Food·Drug·Cosmetic Law

Journal

The editorial policy of this JOURNAL is to record the progress of the law in the field of food, drugs and cosmetics, and to provide a constructive discussion of it, according to the highest professional standards. The FOOD DRUG COSMETIC LAW JOURNAL is the only forum for current discussion of such law and it renders an important public service, for it is an invaluable means (1) to create a better knowledge and understanding of food, drug and cosmetic law, (2) to promote its due operation and development and thus (3) to effectuate its great remedial purposes. In short: While this law receives normal legal, administrative and judicial consideration, there remains a basic need for its appropriate study as a fundamental law of the land; the JOURNAL is designed to satisfy that need. The editorial policy also is to allow frank discussion of food-drug-cosmetic issues. The views stated are those of the contributors and not necessarily those of the publishers. On this basis, contributions and comments are invited.

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REPORTS

TO THE READER

Meeting of Food and Drug Men

On November 24 and 25, 1958, a conference to discuss the 1958 food-additives amendment of the Federal Food, Drug, and Cosmetic Act was held in Washington, D. C. The meeting, which took place in the auditorium of the United States Department of Health, Education, and Welfare, was cosponsored by the United States Food and Drug Administration and The Food Law Institute, Inc., of New York City. Proceedings of the sessions (formal statements and papers and a report) are published in this issue of the JOURNAL.

Moderator of the first session, on the morning of November 24, was **George P. Larrick,** Commissioner of Food and Drugs. Following his introductory statement, initial comments were made as follows: for The Food Law Institute, Inc.—**Charles Wesley Dunn,** president; for the Manufacturing Chemists' Association, Inc.—**Marx Leva,** general counsel; **Lawrence A. Coleman,** chairman of the association's food-additives committee; and **John H. Foulger, M. D.,** a member of that committee.

In a general discussion of the amendment by FDA representatives, **John L. Harvey,** Deputy Commissioner, spoke on its administration; **William W. Goodrich,** HEW's Assistant General Counsel, outlined rule-making under it; **Arthur A. Checchi,** assistant to Mr. Harvey, spoke on its requirements and the proposed regulations; and **Winton B. Rankin,** assistant to the Commissioner, took up the problem of color additives.

At the November 24 afternoon session, **Robert S. Roe,** Director of the Administration's Bureau of Biological and Physical Sciences, presided over an official scientific discussion of the amendment. Among the speakers whose formal papers are included here were the following: Mr. Roe, whose topic was "Scientific Disciplines Used in Evaluating Food-Additive Petitions"; **O. G. Fitzhugh,** Chief of the Toxicity Branch, Division of Pharmacology, who participated in a panel discussion of pharmacological data on food additives; **G. G. Slocum,** Director of the Division of Microbiology, **L. M. Beacham,** Assistant Director of the Division of Food, and **L. L. Ramsey,** of that division, in a panel discussion of chemical data on food additives (Dr. Slocum was chairman of the panel); and **E. M. Nelson,** Director of the Division of Nutrition, and **O. L. Kline,** Director of Research, Division of Nutrition, in a panel discussion of nutritional and medical evaluation of food additives (with Dr. Nelson as chairman).

The third session, on the morning of November 25, went on to further scientific discussion of the amendment and related matters. **Bernard L. Oser,** president of Food and Drug Research Laboratories, Inc., served as moderator, and also presented a paper on challenges to science posed by the amendment.

Other speakers included **F. N. Peters,** vice president of The Quaker Oats Company, on "The Scientific Significance of the Amendment to the Food Manufacturing Industry"; **R. C. Sherwood,** vice president of Sterwin Chemicals, Inc., on "Scientific Problems Under the Food-Additives Amendment, Illus-

trated by Color and Flavor Additives"; **John A. Zapp,** Director of Haskell Laboratories for Toxicology and Industrial Medicine, E. I. du Pont de Nemours & Company, Inc., on "Scientific Problems Under the Amendment with Respect to Food Packaging"; and **Lloyd C. Miller,** director of revision of the *United States Pharmacopoeia,* on "Common Label Names for Chemical Food Additives."

The latter discussion included a preliminary report by an *ad hoc* FLI committee on food-additive nomenclature. Members of the committee are John S. Andrews, director of food research, General Mills, Inc.; Leonard T. Capell, of Ohio State University; Walter H. Hartung, of the Medical College of Virginia; O. L. Kline; Lloyd C. Miller; Kenneth A. Mulford, attorney for Atlas Powder Company; Harvey K. Murer, director of research, General Foods Corporation; A. J. Nydick, lawyer; and Bernard L. Oser, chairman of the *ad hoc* committee.

The session was concluded with an address on food-additive liaison between industry and government through the National Research Council Food Protection Committee, by **David B. Hand,** vice chairman of the committee, of the Division of Food Science and Technology, New York State Agricultural Experiment Station.

At the end of each session, written questions from the floor could be filed with the moderator, to be answered at the fourth session, on the afternoon of November 25. The following FDA panel devoted this final meeting to answering the inquiries, which represented industry, professional and consumer segments: Commissioner Larrick; Deputy Commissioner Harvey; Mr. Goodrich; Mr. Checchi; Mr. Rankin; Mr. Roe; A. J. Lehman, M. D., Director of the Division of Pharmacology; Mr. Beacham; and Dr. Nelson. Moderators for this session were Commissioner Larrick and Mr. Dunn. Questions and answers from this meeting will appear in next month's JOURNAL.

Other government representatives who spoke before the various sessions of the meeting included Bertha S. Adkins, Undersecretary of Health, Education, and Welfare; Dr. Lehman; A. A. Nelson, Chief of the Pathology Branch, Division of Pharmacology; B. J. Vos, Assistant Director of the Division of Pharmacology; J. W. Cook, of the Division of Food; and W. H. Kessenich, Deputy Medical Director of the Bureau of Medicine.

Also in this issue of the JOURNAL, due to close connection with the subject matter of the conference, are a list of chemicals approved under the Federal Meat Inspection Act prior to September 6, which are exempted from the new amendment, and a list of acceptable materials for plastics intended for contact with federally inspected meat food products. The full text of the proposed regulations under the amendment—with changes to press time—is also presented.

The proposed regulations, which were published in *Federal Register* for December 9, had been signed by Commissioner Larrick on December 3.

On the evening of November 24, The Food Law Institute arranged a dinner at the Sheraton-Carlton Hotel to honor the FDA and the enactment of the food-additives amendment. Guests seated at the head table included Arthur S. Flemming, Secretary of Health, Education, and Welfare; Bertha S. Adkins; Edward Foss Wilson, Assistant Secretary of Health, Education, and Welfare; Bradshaw Mintener, former Assistant Secretary of Health, Education, and Welfare; Mr. Dunn; Mr. Larrick; Mr. Harvey; Mr. Goodrich; Mrs. Harvey W. Wiley; Parke M. Banta, General Counsel of HEW; and W. T. Brady, chairman of The Food Law Institute and president of Corn Products Company.

(Continued on page 859)

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Food·Drug·Cosmetic Law
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Food-Additives Amendment

FORMAL STATEMENTS, PAPERS AND REPORT AT WASHINGTON CONFERENCE ON NOVEMBER 24-25, 1958, COSPONSORED BY FDA AND FLI, TO DISCUSS 1958 FOOD-ADDITIVES AMENDMENT OF FEDERAL FOOD, DRUG, AND COSMETIC ACT

INTRODUCTORY STATEMENT

by

George P. Larrick

IT IS A PLEASURE to welcome you to this industry-government conference to consider the new food additives amendment to the national pure food and drug law. We worked with many of you over the past few years as this legislation was considered by several Congresses. We became acquainted with your problems and you with ours. Now we have a law on the statute books which represents the decision of the Congress, based upon the recommendations all of us made. The law differs in some respects from the bill that our Department drafted and submitted to the First Session of the Eighty-fifth Congress but we believe that it is a good law; we believe it places

adequate safeguards around the use of new chemicals in modern processing techniques.

The law differs in some respects from the bills that industry drafted and proposed to the Congress. We understand that it was considered by various industry groups immediately before its enactment and that they also concluded that it is desirable legislation.

Now that the long legislative consideration of food additives has terminated, it is most appropriate that we sit down together to discuss the administration of the new law and to be sure that each of us continues to understand the other's problems and his objectives.

The Food Law Institute, through Mr. Charles Wesley Dunn, requested this conference before the amendment passed Congress. The subject would have been timely in any event but it is doubly so in view of the subsequent Congressional action. We know the exchange of views will prove worthwhile to us. We hope you will find it profitable, too.

I wish there were time to recognize each of you by name and introduce you to the group, but it is evident from the size of the conference that this would consume much of the time available today. Won't each of you accept our sincere welcome just as though it were given individually?

We see a number of representatives of consumer organizations. It is gratifying to have this evidence of your continuing interest in food additives.

We are glad to see William T. Brady, chairman of The Food Law Institute, the many members of The Food Law Institute who are present, and the representatives of other groups that are likewise deeply concerned with the successful administration of the amendment. We extend thanks particularly to the Manufacturing Chemists' Association and to its representatives who are here, some of whom will participate formally in this morning's program.

Originally, The Food Law Institute suggested that the Food and Drug Administration present the first day's program and industry the second. However, it developed that the members of the Manufacturing Chemists' Association were already committed to attend an imporant meeting in New York tomorrow. We want to hear from them and have arranged for Messrs. Leva and Coleman, and Dr. Foulger—representing that association—to speak this morning. We regret that

they cannot be present tomorrow as well, but understand fully the necessity for their leaving.

I now recognize Mr. Charles Wesley Dunn, the man who suggested this conference, and who has devoted a tremendous amount of time to insuring its success.

INITIAL COMMENTS—FOR FOOD LAW INSTITUTE

by

Charles Wesley Dunn

a

This is in effect a joint conference between the FDA, which administers the food additives amendment before us, and representatives of the food and chemical and other industries, which are regulated by this amendment, to develop a required mutual understanding of its compliance and administration in the first instance. The attendance further includes other interested government (both federal and state), professional and consumer representatives, for a completion of its national character. I do not recall a larger or more important Washington conference on our national pure food law; with the exception of the 1956 one to commemorate its fiftieth anniversary.

The conference is a timely one, because this amendment was recently enacted on September 6 and is now at the threshold of its effective career. It is also an essential conference, because this amendment presents infinite legal and scientific questions in the long view; and the legal questions will doubtless require more or less judicial answer in that view. The conference program has been organized to record necessary initial answers by the FDA, on the application and operation of this amendment; and they will constitute a primary working manual thereon, for general use. The program also contains an important preliminary report by an *ad hoc* FLI committee, on simple label names for complex food additives.

I should note here that The Food Law Institute has just published the legislative record of this amendment, through the Commerce Clearing House in Chicago (4025 West Peterson Avenue); which has a lasting reference value. For it contains annotating statements by Congress, which define the amendment's intent in basic and other respects.

Orders for this record should be addressed to the CCH; and the price is $3.00 per copy, with a lower quantity price. I also note that the proceedings of this conference will be published by the CCH in the FOOD DRUG COSMETIC LAW JOURNAL, beginning with the December issue.

b

Turning to the amendment itself: Since the FDA will later examine it in detail I will now simply and quickly recall its general purpose and outline, as a basis for some introductory comments. This amendment revises the old law of the Federal Food, Drug, and Cosmetic Act, providing for the safety of manufactured food additives; and they mainly include chemical additives, beneficially used to improve the production and character and value of such food. That law is revised for a three-fold purpose. It is (1) to regulate the safety of manufactured food additives before (instead of after) their use, for a required better protection of public health; (2) to authorize the use of beneficial chemical additives at safe levels which are otherwise unsafe, for essential progress in food technology to improve the food standards of living; and (3) to strengthen that law otherwise. I note that as so revised the old law is expanded from a few lines to numerous pages.

The amendment effectively accomplishes these purposes. For in the first place and subject to indicated exemptions this amendment broadly applies to any old or new substance intended to be used in the manufacture of any human or animal food (including a drink) and affecting the composition or any characteristic of it, which is potentially unsafe under the conditions of its existing or intended use. That is a scientific question to be determined pursuant to a strict "generally recognized" test, with any substantial doubt resolved in favor of this protective amendment. But that question does not arise in the case of old substances used in food prior to January 1 last, whose safety has been adequately established by the experience of their common use in food; and this is a question of fact to be appropriately determined in each instance. Hence it may be said that the amendment will deal mostly with new additives and more occasionally with old ones. Furthermore the amendment will also apply to any potentially unsafe substance indirectly added to such a food in its manufacture or through its packaging or because of the conditions under which it is held or transported, where that addition may reasonably be expected; and this is likewise a question of fact to be determined in each instance. I note that the provision against a packaging contamination of food sup-

plements the container one now in the FDC Act; that the responsibility for preventing this contamination originally resides in the manufacturer of a food container or wrapper; and that a food manufacturer should obtain a compliance guaranty from him. As to the exempted additives: they principally include chemical ones to the extent their use was administratively approved under the Federal Food, Drug, and Cosmetic Act, the Federal Meat Inspection Act and the Federal Poultry Products Inspection Act, respectively, prior to September 6 when the amendment before us was enacted; but I note that this approval may be hereafter revoked or modified thereunder for cause. It follows that advisory lists of these exempted additives should be forthwith published on a thus classified basis for the guidance of all concerned, except where their publication violates a trade confidence or reveals a trade secret protected by the FDC Act. This exception mainly applies to chemical additives then informally approved under the FDC Act; and it does not apply to such additives that were formally approved thereunder, in food standards of identity.

It is clear that the foregoing questions presented by this amendment create difficult problems of its construction, because their solution is governed by general legislative principles. Therefore FDA advisory cooperation is needed for their due industry solution; and this conference is a first step in it. Moreover I should pause here to make the following important point: whatever may be the number of manufactured food additives found to be potentially unsafe under this amendment, which is now unknown, they will be limited exceptions to the general rule otherwise. For this rule is that manufactured food additives, mainly of farm and agricultural origin, are normally safe by reason of their very nature and as proven by their long common use; and that our people actually enjoy the highest standards of pure and safe and wholesome food, created by a responsible and superb food industry. The legislative record of this amendment confirms the aforesaid general rule. Consequently for these reasons and also because this amendment is principally designed and mostly effective to prevent what it prohibits, we should be careful that our discussion of this amendment does not impair public confidence in such rule.

c

In the second place this amendment strongly regulates the use of any manufactured food additive which is thus potentially unsafe, mainly and substantially as follows in terms and effect: It first makes

two industry requirements, which on their face normally apply to the producer of such additive. The first requirement is that the additive must be adequately tested or pretested by an appropriate scientific procedure to establish that it is actually safe under the conditions of its existing or intended use, as the case may be. This requirement is the amendment's basic and definitive one, as the title of its act expressly indicates; and that is why it is commonly known as a "safety pretesting amendment", referring to its major objective. I note that legitimate food and additive manufacturers voluntarily recognized this requirement before it was enacted, because they must responsibly act to assure the safety of essential food; and therefore this amendment has the primary significance of converting a voluntary industry requirement into a mandatory legislative one, to prevent any injurious failure or neglect otherwise to comply with it. As to the second requirement: it is a supplemental one that if the foregoing testing or pretesting of such additive apparently establishes that it is safe under the conditions of its existing or intended use, as the case may be, a petition must be filed with the FDA which proposes a consequent administrative regulation issued under this amendment and prescribing the conditions under which the additive may be safely used; and which contains the supporting testing or pretesting and other required data. Therefore a notice of this proposed regulation must be administratively issued, "in general terms".

The amendment next provides: the FDA must fairly evaluate the aforesaid and other pertinent data before it, to determine whether the additive in issue is actually safe under the conditions of its existing or intended use, as the case may be. Thereafter the administrator of the FDC Act, proceeding on FDA advice, must by order deny the petition or establish a regulation prescribing the conditions under which the additive may be safely used; he must notify the petitioner of this order and the reasons for it; and he must forthwith publish the order, which is then effective unless it is stayed for a requested administrative review later explained. I note that such a regulation may deviate from that industrially proposed, if and to the extent the FDA finds this deviation necessary to protect the public health; and that it may broadly define the conditions under which its additive may be safely used, as provided. I also note that such a regulation may prescribe a maximum safe limit on the quantity of its additive, if this limit is based on a fair administrative evaluation of the related data, it is not higher than is reasonably necessary in the circumstances,

and it satisfies defined conditions. I further note that such a regulation has a general industry force, subject to any patent or secret process limitation on the use of its additive; that it is governed by strict standards for its issuance; that it may be administratively amended or repealed as subsequently required; that it is open to an administrative and judicial review as provided; and that an order issued in an administrative review proceeding must be based on a fair evaluation of its entire record.

The amendment then closes its protective door by broadly prohibiting any interstate or foreign commerce in any manufactured food additive which is subject thereto, or in any food bearing or containing such additive, unless it and its actual or intended use conform with an effective administrative regulation issued thereunder and prescribing the conditions under which the additive may be safely used. This prohibition became effective on September 6, when the amendment was enacted; but the foregoing industrial petition requirement is postponed until six months after that date, although it may be voluntarily met in the interval; and that postponement is further extended as provided, in the case of an additive's particular commercial use before January 1 last. I note that such interstate commerce prohibition is complete; whereas the foreign commerce one is subject to a general exemption in the FDC Act, which may be used to defeat it; and therefore Congress will perhaps review that exemption, because the parallel new drug law of the FDC Act is not subject to it. I also note that the above interstate and foreign commerce prohibition, taken as a whole, is enforced by the criminal and seizure and injunction proceedings authorized by this Act; and that in each proceeding the burden is on the government to prove a violation of the prohibition, to the required degree. Hence while this amendment requires the producer of a subject food additive to make a safety testing or pretesting of it as provided (etc.), the burden still remains on the government to prove his violation of the amendment in an enforcement proceeding against him with respect to it. I should go on to say that a food manufacturer should of course obtain a protective compliance guaranty from each of his additive suppliers, which is authorized by this Act.

We now have the principal regulatory law of this amendment before us, which has the industrial origin described; and I should add several further comments on it. They are: (1) Such law presents

many important procedural and administrative questions of detail, which invite initial FDA answer at this conference to the full available extent. (2) While this law is a strong one as enacted, its practical effect will be determined by the industry approach to it and the FDA administration of it. Manifestly the former approach should be a constructive one, in harmony with this amendment; whereas the latter administration should be a sound, fair and effective one, which maintains a due balance between the amendment's purpose to protect the public health and its supplemental purpose to further a beneficial industrial use of safe manufactured food (especially chemical) additives, which are needed or valuable to develop higher food standards of living. (3) This amendment safeguards trade production secrets as provided, which are necessarily revealed to the FDA in its administration; and the regulation thus authorized is strictly confined to prescribing the conditions under which its additive may be safely used. (4) While this amendment principally authorizes a regulation of industrial origin, it also vests in its administrator the supplemental authority to issue a similar regulation, on his own initiative and with respect to any particular use of an additive and where required to protect the public health, prescribing the conditions under which the additive may be safely used; and it is likewise open to the administrative and judicial review aforesaid. That authority is in the nature of an emergency one, for exercise if and as needed.

d

In conclusion: this amendment marks the most important advance in our national pure food law to assure the safety of manufactured food, since its original enactment more than half a century ago. And our outline of it establishes that it is more a scientific amendment, which explains the scientific weight of this conference program.

Two related problems remain. The first is for Congress to provide the appropriations required for a due administration of this amendment. The food manufacturing industry (for example) should cooperate in securing these appropriations, since it has a basic stake in a duly organized and conducted administration of this amendment; and it should also cooperate in securing the appropriation increases required to administer the FDC Act generally, which the Citizens Advisory Committee recommended. The second problem is to make certain that any similar amendment of the state (including municipal) food laws is strictly uniform with the federal one before us; whereby

a compliance with the federal amendment is automatically a compliance with each like state amendment.

In view of the fact that this food additives amendment of the FDC Act has opened an entirely new and very important era of food law regulation creating the foregoing and other significant problems, The Food Law Institute has established a public advisory committee to aid it in constructively dealing with them. Its members presently include Mrs. Grace D. Nicholas, Executive Director of the General Federation of Women's Clubs, Dr. Charles Glen King, Executive Director of The Nutrition Foundation, Colonel Charles S. Lawrence, Executive Secretary of the Institute of Food Technologists, Charles A. Feld, Executive Director of the Packaging Institute, Inc., Dr. Austin Smith, Editor of the *Journal of the American Medical Association,* and Dean William C. Warren of the Columbia University Law School. Other members will be added in due course.

—FOR MANUFACTURING CHEMISTS' ASSOCIATION

by

Marx Leva

GENERAL JOHN E. HULL, president of the Manufacturing Chemists' Association, has asked me to express to all of you his regrets over his inability to attend these sessions today and tomorrow. Unfortunately, the annual midwinter meeting of the Manufacturing Chemists' Association is being held in New York on these same dates, so not only General Hull, but also many other leaders in the chemical industry who would otherwise be present here today, have found themselves unable to master the age-old problem of how to be in two places at the same time. In General Hull's absence, you will note from your program that three of us—Leva, Coleman and Foulger—are representing the Manufacturing Chemists' Association at this opening session of the highly important and significant two-day meeting which the Food and Drug Administration and The Food Law Institute have arranged.

Mr. Lawrence Coleman, chairman of the food-additives committee of the Manufacturing Chemists' Association and general counsel of Allied Chemical Corporation, will follow me at the speaker's stand and will discuss the concept of "safety under the conditions of in-

tended use," as enacted into law by the food-additives amendment of 1958. Dr. John Foulger of E. I. duPont de Nemours & Company, a member of MCA's food-additives committee and one of the country's leading toxicologists, will follow Mr. Coleman and will discuss the great importance, under the new law, of avoiding any "freezing" of the science of toxicological testing.

Since I am to be followed by two such experts, I will make my own remarks very brief and will address myself primarily to the chemical industry's attitude towards the new law as a whole. Perhaps the best way for me to begin such a discussion is by quoting briefly from a letter which General Hull, as president of the association, sent to Chairman Hill of the Senate committee and Chairman Harris of the House committee during the closing days of the recent Congress. In his letters to the committee chairmen, General Hull said:

> We hope this bill . . . to prohibit the use of food additives which have not been adequately tested to establish their safety . . . will be enacted into law prior to the adjournment of the present session of Congress.

In his letter to Chairman Harris, General Hull also said:

> From our interest and experience in this important field we believe, as we have testified before your Committee on two occasions, that there is a very real need for modern amendments to the Food, Drug, and Cosmetic Act to clarify and augment the procedures under the Act so as to achieve greater protection for the public health, and at the same time to permit scientific development of further improvements in the Nation's food.

Having advocated the enactment of legislation in this field for a number of years and having urged that the Congress not go home this past summer until it enacted the specific bill that became the food-additives amendment of 1958, the chemical industry is gratified that the new law is now a *fait accompli* on the statute books.

I stress our industry's long-standing support of the need for such a law because I think it is important to realize that the chemical industry, like the food industry, has for many years advocated federal legislation to plug the loophole or gap that existed in our federal food and drug law prior to the enactment of this legislation.

Just about four years ago, in a speech before the Section on Food, Drug and Cosmetic Law of the New York State Bar Association, the president of the Manufacturing Chemists' Association stressed the desirability of prompt Congressional action in this area. More recently, in testimony presented before the House Interstate and Foreign Commerce Committee in 1956 and, again, in 1957, the chairman of MCA's food-additives Committee—James Gillet, in 1956, and Lawrence Cole-

man, in 1957—have urged the enactment of legislation which, in substantive content, was very similar to the legislation which Congress finally enacted in 1958.

I would not like to leave the impression that the legislation that has now been enacted is precisely the same as the legislation which we have been advocating over the years. The essence of the legislative process is compromise—and I think I can state with complete accuracy that the law that has finally emerged contains many of the features that the chemical industry has been advocating and contains also many features that others, including the Food and Drug Administration, have been advocating.

Nowhere is the compromise nature of the legislation clearer than in its judicial-review provisions. At the risk of oversimplification, I would say that industry would have preferred legislation under which the Food and Drug Administration's enforcement authority would have taken the normal route of *judicial* action initiated by the Food and Drug Administration in the district courts, to be followed—where necessary—by resort to the courts of appeals. The Food and Drug Administration, on the other hand, would have preferred an enforcement procedure based almost entirely on *administrative* action—specifically, a procedure whereby FDA's administrative action would have been final, to all intents and purposes, subject only to a highly restricted type of appeal to the courts of appeals.

The legislation that has emerged compromises these two conflicting viewpoints by providing for *administrative* enforcement in the first instance, but with a broad right of *judicial* review in the courts of appeals under a procedure which specifies that the Food and Drug Administration, in order to sustain its administrative action, must satisfy the court that the administrative action was based on "a fair evaluation of the entire record."

Commenting on this provision of the new law, the Senate Committee on Labor and Welfare (in its report recommending that the Senate enact the measure) said: "The specific language of this bill—'fair evaluation of the entire record'—represents a new standard of judicial review." The Senate committee, in this same report, described this "new standard of judicial review" as a "significant change in existing law."

It was this type of constructive compromise which cleared the way for the enactment of the new law. The Food and Drug Administration

and, in particular, Commissioner Larrick and those closely associated with him in this matter deserve great credit for the patient and painstaking work, and the corporation with industry, with consumer groups and with the Congress, without which there would never have been a food-additives amendment of 1958. On behalf of the Manufacturing Chemists' Association, I am glad to be able to participate in this program today and to express the appreciation of the chemical industry not only for the cooperation which FDA extended to industry while the legislation was pending before Congress, but also for the cooperative manner in which FDA is approaching the problem of its regulations and procedures under the new law.

—FOR MANUFACTURING CHEMISTS' ASSOCIATION

by

Lawrence A. Coleman

MR. LEVA has rightly given emphasis to the major *jural* innovation appearing in the food-additives amendment of 1958, that is, the special form of judicial review in the United States Court of Appeals for which it provides. Those of us who were close to the legislative evolution of the amendment remember well the critical examination given this provision by all concerned. Together with the pretesting requirement and the "conditions of intended use" standard, it forms the very core of the Act.

As to the standard which relates safety to conditions of intended use, I would underscore one related point which deserves particular mention. In the final analysis, the crucial operative provision in the administration of the law is that section which confers upon the Secretary the power to fix tolerances where necessary to assure the safe use of a proposed additive. I am sure the Secretary of Health, Education, and Welfare and the Food and Drug Administration is not unmindful of the fact that this grant of power is an enormous one. It is not inappropriate to allude to something John Marshall once said,* if somewhat differently: "The power to fix tolerances involves the power to destroy."

The Secretary's power to fix tolerances is a power which, for reasons inherent in administrative law, is one not amenable to exten-

* *M'Culloch v. Maryland*, 4 Wheat. 315, 431 (1819).

sive judicial review. Nevertheless, it is clear that the law imposes specific limitations on that power which, if not observed, form a basis for judicial review. The power must, therefore, be exercised responsibly. Thus, the Act provides that if in the judgment of the Secretary a tolerance limitation is required in order to assure the safety of a proposed use of an additive, he may fix such a tolerance. But, the Act continues, in determining whether a proposed use is safe the Secretary *shall* consider (notice the word "shall") the probable consumption of the additive, the cumulative effect of such additive *in the diet,* and safety factors.

It seems plain that the power to fix tolerances *must* be exercised—and I repeat the word "must"—as a function of the probable consumption of the additive *in the whole diet.* The failure of the Secretary to observe this directive of the Act—in other words, the fixing of a tolerance with regard only to the artificial diet of a test animal—is a basis for setting aside his order.

Now this is only as it should be. In fixing a tolerance, it cannot normally be supposed that the concentrations of an additive present in the testing procedure are concentrations present in the whole diet. This cannot be true except in the rarest instances. It is only sensible, therefore, to require, as the Act does, that the laboratory no-harm level be translated into a tolerance which relates the additive to the total diet. To wield the power to fix tolerances in any other way might well mean the exercise of a power to destroy, that is, the destruction of the utility of food additives.

While the Act places this burden upon the Secretary, it implicitly places a corresponding burden on industry. It is clear that if the Secretary is to be effective in relating tolerances to total diet, comprehensive data must be made available to him of the many use levels of a given food additive in different foods.

As these data are most easily available to the industry, the normal rule of law would by analogy suggest that the burden of proof be borne by industry, that is, that industry be responsible for the collection of these data; the Act itself, it seems, is silent as to this specific point. It would be well, then, if industry were to collect this information where it is presently lacking. It will be incumbent on the administration to accept and evaluate these data.

I would make one final observation. The Act authorizes the Secretary to fix labeling or packaging requirements for an additive

where necessary to assure safety of use. I am quite sure that Dr. Oser's labeling committee, when it reports tomorrow, will have much of value to contribute to our discussion of this subject. There is, however, one point which is surely crucial to any consideration of the question: The ultimate success of a label is measurable *not* in terms of its fidelity to scientific principles, but rather in relation to its *meaningfulness*. Labels are signals. They present a problem of communication, not of chemistry. Accordingly, their effectiveness must be gauged, like a radio transmission, by the capacity of the receiver to receive. The receiving equipment of a food consumer is not so attuned to 2, 3-idhydro-3-oxobenzisosulfonazole as it is to "saccharin," and labels should reflect this consideration. Where the common name of an additive is not so well known, adequate protection is afforded by the use of the generic class name of the additive: antioxidant, preservative, surfactant, and the like.

We are here today to witness the dawn of a new era in the food law of our country. Let me note how privileged I feel to be present in this auditorium on this occasion.

We are all, surely, in the debt of Mr. Dunn and Commissioner Larrick for having made possible the free exchange of views, and the attendant clarification of the law, which will doubtless be the fruit of this conference.

—FOR MANUFACTURING CHEMISTS' ASSOCIATION

by

John H. Foulger, M. D.

WE ARE HERE TODAY to discuss a public-health law. Its success in protecting the public depends to a great extent upon application of modern medical science to toxicologic testing.

For almost 18 years there has been close cooperation between the chemical industry and the Food and Drug Administration, with mutual exchange of ideas on methods of testing for safety and with discussion of data given by those procedures. During that time, Dr. A. J. Lehman and his staff, of the Division of Pharmacology, quite properly have published details of a testing program. This has been of great benefit to everyone concerned. However, with voluntary testing now made mandatory, a published program from such a source takes on a new aspect.

During the discussions of the scientific panel before the House committee in August, 1957, I offered the opinion that, whatever form a new amendment to the food sections of the Federal Food, Drug, and Cosmetic Act of 1938 might take, there should be no "freezing" of testing procedures, for this could have important and serious consequences. I am here this morning to repeat that statement and to enlarge upon it.

First, if a program of testing should become rigid, scientific review of an application under Section 409 of this new law could become virtually impossible, since emphasis would be on compliance with administrative routine rather than on scientific merits. It is even remotely possible that a clerk would check the items in the testing procedures of the application against a standard list; it might thus come to pass that omission of one or more items administratively required would be considered as evidence of inadequate testing.

Second, a rigid, standardized testing program would tend to discourage creative thinking in the field of toxicology. This would be very detrimental to public interest. A monotonous routine discourages original thought and encourages mediocrity.

Again, some of us who have had many years of experience in the study of the influence of chemicals upon health have come to feel that the present program does not provide information proportionate in value to the effort and time expended. Even after spending two to three years in testing for safety, it is deemed necessary to apply a safety factor as high as 100 to the results of the toxicologic program.

I am not making this criticism of the current testing program merely to be captious nor without suggesting any substitute approaches. Here are two which have interested me for the last 12 months:

The *Federal Register* of Thursday, August 21, 1958, published tolerances for a number of insecticide residues on agricultural products. It is interesting that the numerical value of many of these tolerances is closely matched by the natural logarithm of the oral LD50 of the compounds concerned. The "tolerances" of many others fell below the logarithm. Now, no one would suggest that a tolerance could be based solely on an acute test to determine the LD50 plus a table of logarithms. But this relationship might be of considerable value. For example: If, when the LD50 test is completed, one finds that its logarithm has a numerical value far below the concentration of the additive necessary to perform the function which one desires,

then obviously one should decide whether or not to abandon the development of this material. At the moment there is no good guide for such a decision. Again, in planning the long-term toxicity tests, one might with profit use the logarithm of the LD50 as one level in the food and so decide whether this is actually a "no effect" level.

There is another approach which is interesting. Many chemicals strongly inhibit important enzyme systems. It is interesting that if the LD50 of these chemicals is represented as an instantaneous blood concentration in gram molecules per liter, this concentration is in general of the order of ten times the concentration known to have a strong inhibiting action on important enzymes when tested outside the body. It is characteristic of chemical inhibition of enzymes that the process is reversible. Further, there is a "no effect" level of the inhibiting agent. A study of the action of chemicals on enzyme systems might, therefore, be very rewarding, giving information not obtainable by routine measurement of organ or body weights.

I am mentioning these two procedures in brief merely to show that there are other approaches to the problem than that presented by the present program of testing. Undoubtedly, concentrated study will disclose many new and far better procedures. But such studies will be discouraged and even fruitless if the current program of testing should be frozen by regulation.

On the contrary, the science of toxicology could take on a new lease of life if a regulation should issue making it clear that the administration will not demand or even endorse a particular program of testing. Endorsement of a program outlined by an international committee might make matters very difficult. Such committees meet seldom; the membership varies from time to time and varies greatly in individual background. Such committees would be rather slow to move in conformity with modern research.

If it should be made clear that safety testing procedures must depend upon the specific properties of the additive under study, that no particular program is demanded but that tests used must, in fact, show the additive to be safe under conditions of intended use, we can move forward to advances in toxicology which will benefit the public, the physician, the manufacturer and the administrator. The problems of the influence of new chemicals on human health go far beyond the field of food additives. In fact, they enter into all phases of modern preventive and clinical medicine.

ADMINISTRATION OF THE FOOD-ADDITIVES AMENDMENT OF 1958

by

John L. Harvey

THE food-additives amendment is a relatively simple law. We are now beginning a two-day discussion of it and are confronted with the danger of making it seem complex by reason of having so much to say about it. It is my sincere hope that in our discussions we shall not oversimplify this important legislation and also that we shall not make the whole subject sound so involved that you may conclude that "there is no way to get from here to there." It is our hope that the proposed regulations which are being made available here will not be regarded as overly complex.

With regard to these proposed regulations I think I should say that it is our hope that we shall receive the fullest possible discussion and comment and that the proposals will not be regarded as representing final and fixed views of the Food and Drug Administration and that, further suggestions and advice from all concerned will not be given full consideration.

We believe that it is incumbent upon us to develop final regulations prior to the effective date of March 5, 1959. We hope that the publication of these proposals will bring forth a full expression of viewpoints from all who are regulated by this law.

In administering the amendment, we expect to be guided by the same principles which we employ in the over-all administering of the provisions of the food and drug law. We have a grave responsibility to the consuming public to carry out effectively the intent of the law. This intent is expressed in the title "To prohibit use in food of additives which have not been adequately tested to establish their safety." At the same time, we have a duty to the manufacturing industries to achieve this objective within the framework of the law with complete fairness and with the minimum of added burden that will accomplish the objective. In a sense, the responsibility for the effective administration of the law is shared by the Food and Drug Administration and by the manufacturers of additives and of the

foods in which they are used. I think we also have a shared responsibility to keep the consuming public advised of actions taken and the reasons for taking them. Consumers have a right to know what is going into their food. They have a right to know that the additives that are permitted in their food supply are safe and are used to accomplish physical and technical benefits. They also have a right to be relieved of the fears that have been built up in the past few years—many unreasoning fears about the safety of our food supply. We expect to give accurate information to the consumer about our activities under this law, and we solicit the cooperation of all industry to the end that unwarranted alarms not be created and that unreasoning fears be allayed.

We do not expect unnecessarily to reveal and make public secrets which are entitled to protection. We must publish proposed and final regulations which are sufficiently specific to meet the test that they clearly and adequately inform as to what can be done and what cannot be done. The provisions of these regulations are instruments of law enforcement and cannot be vague and uncertain. This, however, means nothing more than to say that the regulations must clearly identify the additive as to exactly what it is and must clearly set forth the quantities that may be employed and the food in which it may be used, together with such conditions of use as may be necessary. You know, of course, that except in a few specified instances the law requires the ingredients of food to be stated on the label.

I realize that there is a great deal of concern among some segments of industry that this amendment may be an instrument of revealment of secrets which will be devastating to manufacturers and a boon to their competitors. I do not share this view at all and I assure you unequivocally that it will be our purpose in administering this amendment to avoid any such unfortunate by-products in every way possible under the law. We shall always be willing to discuss any problems of this kind about which you have concern. Rather than believing that the amendment will prove disadvantageous to manufacturers, it is our view that it will result in a restoration and increase of public confidence in our food supply and will facilitate the development and marketing of new products.

The judgmental decision as to how much of what may be allowed in food is essentially a scientific one. It is not in our view an academic scientific decision, but is a decision to be made by working scientists

who are actively engaged in study and research in the particular scientific field.

Our plans are to provide significant augmentation of the technical staff of our scientific laboratories to supplement the services of the high-caliber scientists who are already in the Food and Drug Administration. We must have adequate laboratories and adequate qualified scientists to perform the research studies which are necessary to make sound scientific decisions, and we must, of course, have adequate, competent administrative staff to complete the operation of providing the regulations for use of additives.

We have no immediate problem in financing the new amendment. Immediately upon its passage the Secretary of Health, Education, and Welfare took steps to obtain authority for the financing of the job through deficit spending to be met by supplemental appropriation from the next Congress. This was necessary because the timing of the passage of the amendment would not permit appropriation for it by the Eighty-fifth Congress. This is not a situation in which we are called upon to take on additional duties under new laws without having obtained funds to permit us to discharge the new responsibilities.

It is, of course, difficult accurately to determine precisely the augmentation of staff that will be necessary. We have requested funds which we consider essential, and we believe now that the amount made available will suffice for the current year—so I may say to you that we have developed tentative or proposed regulations. We have determined the basic and fundamental philosophies which will guide us in the administration of the amendment. We have obtained for the time being the necessary financing. We will vigorously move forward to obtain and develop the necessary augmentation of personnel. We are prepared at the present moment to deal with petitions as they are submitted. We believe that we shall be fully prepared to deal with the rush of business that inevitably will arise when the amendment becomes effective in its mandatory provisions on March 5, 1959.

We are undertaking to expand our interdepartmental understandings further to facilitate the carrying out of the provisions of the amendment. You recognize, of course, that working agreements and relations must be maintained between the Food and Drug Administration and the United States Department of Agriculture because

of the interrelationship between the additives amendment and the meat-inspection and poultry-products-inspection laws. You will recognize that working relations must be maintained with the Alcohol Tax Unit of the Department of the Treasury, since alcoholic beverages are food and since additives used therein are subject to the provisions of this amendment. There is an impingement upon the activities of the Atomic Energy Commission, since this amendment is designed to include the use of products of fission and fusion in connection with the production of our foods. These intergovernmental agreements and understandings are being worked out.

We have taken into account the fact that products which may become food additives are also subject to other provisions of the Federal Food, Drug, and Cosmetic Act. We recognize that a product intended to be fed to animals is a drug or a new drug and may become a food additive if the effect of its being fed to animals is to produce meat, milk or eggs which contain components derived from the additive used in the feed. We have outlined a procedure that will make it necessary for new drugs or additives of this nature to be dealt with only once. If a new-drug application is filed and it is apparent, from its nature, that it must also be considered under the food-additives amendment, it will be so considered.

We have not made new-drug applications effective for veterinary products where there may be a residue carried over into meat, milk or eggs unless there have been submitted with the new-drug application adequate data on the residue in the food product. This situation is unchanged by the amendment, although a single petition may lead to an effective new-drug application and a regulation under the food-additives amendment. Similarly, where an additive is proposed for use in food products which are the subject of standards of identity, both the standard-making operation and the safety of the food additives will be handled as a single operation. In every way possible, we do and shall seek to avoid complexity and to make the problem of securing all clearances necessary as simple as possible for the applicant.

We shall, of course, at all times keep in mind that the purpose of the amendment is to prevent the use in food of additives which have not been adequately tested to establish their safety. We shall, however, continue to maintain our open-door policy and undertake informal discussions at any time, rendering every reasonable assist-

ance to manufacturers in their efforts to secure regulations. I am certain that the vast majority of food manufacturers and most of the manufacturers of chemicals intended for use in foods are quite familiar with the Food and Drug Administration and how the law is administered. I am happy to note that the alarms and concern about the dire effects of this amendment that have manifested themselves in some segments of the affected industries have not been particularly apparent among those who are most familiar with us and with our operations.

We sincerely hope that those who are less familiar with the principles that guide the Food and Drug Administration will recognize that our purpose is to facilitate the utilization of safe food additives and not to obstruct or delay your efforts in any way.

This law clearly recognizes the place of food additives in the food supply and places no barriers to their use except those expressed in the amendment itself: They must be safe under the conditions of use and they must not promote deception or cause violations of other sections of the food and drug law. So long as the proposed additive meets these criteria, we shall share your enthusiasm for getting it into the food supply.

RULE-MAKING UNDER THE FOOD-ADDITIVES AMENDMENT

by

William W. Goodrich

JUST before final passage of the food-additives amendment, we could answer any question posed to us about its meaning and precisely how it would work. But the day after its passage, we had forgotten a great deal that we thought we knew, for we found to our dismay there were many difficult questions for which we had no ready answers. This meeting will certainly bring forward such questions.

The scope of my discussion is rule-making under the new amendment. But since the approval of, or refusal to approve, a proposed use of a food additive must be expressed by a regulation, my subject covers everything that must be done under the new law. Clearly, I could not discuss so broad a subject within the time available. I can only touch the highlights of the rule-making procedures.

The rules to be promulgated under the new law fall into two classes: (1) the general interpretive and procedural rules to place the new law into operation and (2) the rules which will issue thereafter, one by one, as we act upon specific petitions presented to us.

A draft copy of the proposed interpretive and procedural rules will be distributed here to you. We earnestly solicit your comments on them and all suggestions for their improvement.

Broadly speaking, initial regulations cover four subjects:

First, we have included definitions and interpretations and partial lists as to which substances are covered by the new law and which are not and as to the general principles we propose to follow in evaluating the scientific data and in putting it to practical use in insuring the safety of the additive in man's diet. The problem of using animal-experimentation data in estimating the safety of a chemical for man over his life span is a highly specialized one, for which no standard set of tests and standard methods of evaluating the tests can be devised, but we felt that we should start with a clear expression of the basic rules and margins of safety that we propose to apply.

Second, the regulations deal with the interrelationship of the new procedures and our responsibility under the new-drug, food-standards and pesticide-chemicals provisions of existing law. These points are to be discussed in greater detail in other papers.

Third, we have described in considerable detail just what data should be included in a petition for a food-additive regulation, and how we propose to act upon it. In preparing the form, we have drawn heavily on our experience of some 20 years in the new-drug field and our more recent experience under the pesticide-chemicals amendment of 1954. The form for filing petitions is a detailed one, designed to provide the greatest assistance to the petitioner so that all needed information will be in the petition when it is presented to us. This will prevent false starts and avoidable delays. Provision is made, however, for handling incomplete petitions; for supplementing deficient petitions; and for withdrawal without prejudice, when needed supplemental data cannot be collected and submitted within the short periods allowed for our action on petitions.

Finally, the draft regulations take up the filing of objections, the conduct of the public hearing and the problem of judicial review.

We have incorporated the suggestions of the President's Conference on Administrative Procedure to facilitate the hearing, to avoid protracted delays, and to eliminate needlessly long and involved records.

The objection procedure is the point at which we shift from informal rule-making to formal rule-making.

Under the new law, only persons who will be adversely affected by the regulation, if placed in effect, have standing to object and, thereby, to precipitate a formal hearing and a formal ruling on the record. The courts of appeals, under related provisions, have held that a competitor is not adversely affected when regulations permit a person to compete more favorably with him. But one court has held that even a consumer may be adversely affected when he alleges potential harm to himself and to his family. We do not anticipate that persons only casually interested on the basis of theoretical rather than real hazards can demand a formal hearing.

The objector is required by the law to establish reasonable grounds for his objection before it may be filed. This means that he must show he is prepared to produce facts, in the event of a public hearing, which may lead to a result different from the one proposed by the initial regulation. He must show what is wrong with the regulation to which he objects and how he proposes to prove that it is wrong.

The objection procedure is a valuable innovation developed several years ago under the antibiotic certification provisions of the Act, and perfected in the Hale (food-standards simplification) Amendment and the pesticide-chemicals amendment. Its most significant improvement is to identify sharply the controversial issues and to restrict the public hearing to those issues alone.

Perhaps many of you have not thought specifically about what will happen if proper objections are filed and a public hearing ensues. The issue will be whether the Department has properly exercised its scientific judgment in estimating the future hazard to man or animals if a food additive is admitted to his daily diet. All of the underlying scientific data will have been submitted to the Department in the petition and its supplements; the Department will have told the petitioner what its appraisal of the data is; all of the documentary scientific evidence will have been submitted in advance; and the hearing necessarily will be confined to second-guessing the judgment once reached. There can be, of course, a formal investigation into

the reliability of the data at the hearing—including a critical study of reported results and the underlying data on which the reported results rest. Occasionally, facts may be developed which make the entire scientific study suspect or worse. But, in general, the hearing will concern not the data, but adequacy of the data to compel or to support one or another scientific judgment on the safety issue and related questions such as the amount to be tolerated, and whether the additive will accomplish its intended physical or technical effect and will not result in deception of the consumer or in adulteration or misbranding. This is something that is sometimes hard to prove; a sound judgment, particularly on the future safety of an additive, is often more to be felt than proved.

The Congress has told the Department to make a fair evaluation of the entire record and to set forth in detail its findings and conclusions on the record. The committees have said that this is a new requirement, though we have always tried to follow that rule without the precise language. Just what different techniques of record appraisal are intended are not clear to us. The example given in the committee reports is one in which there are opposing conclusions based on the scientific judgment of qualified scientists as to the safety of a food additive. The Department may not rely on the judgment of one scientist, no matter how well qualified, without taking into account the opposing conclusions of other equally qualified scientists. This is a good rule, but it does not mean that one man's judgment may not prevail when it is grounded on more persuasive scientific reasoning from the known facts. It means only that everyone's view must be studied before a final conclusion is reached.

We are told that the decision may not be based on the "personal convictions of scientists employed by the Food and Drug Administration" instead of inferences fairly to be drawn from the scientific evidence of record. Certainly we can agree, wholeheartedly, with that principle, but we do not understand it to disqualify our staff from expressing and supporting its judgment, or the Department from acting on it, when—in the light of the entire record—it is believed to be the sounder judgment on safety.

On judicial review, it has been made plain that:

> . . . one making a rule for the future which in practical effect will determine whether millions of people shall eat something every day may reasonable refuse to subject the general public to even slight risks and small deceptions.

And when the rules must be based on evidence of record at a hearing, the Supreme Court has assured us such evidence includes estimates and forecasts of the probable future effects of present trends. Undoubtedly, the evidence will be evaluated with a conservative approach. If there is any real question from the safety data, it will be resolved against the additive and in favor of the public. But when there is a reasonable certainty that no harm can come from a proposed use of an additive, that use will be permitted.

Drawing on our experience in the handling of almost 11,000 new-drug applications and on four years with the pesticide-chemicals amendment, a formal hearing and judicial review will be a rarity indeed. The rules which will emerge from the new amendment will be, for the most part, products of the scientists' study of submitted data and will reflect the FDA's best scientific judgment on whether a proposed additive will be safe in man's diet.

FOOD-ADDITIVES AMENDMENT—REQUIREMENTS AND PROPOSED REGULATIONS

by

Arthur A. Checchi

ACCORDING to the program, I am supposed to speak on, among other things, the requirements of the food-additives amendment of 1958. Since this has been such a lively topic for discussion during the past few months, the basic requirements of the amendment must be as well known to you as they are to us. Proceeding on that assumption I shall make but a very brief comment on this aspect and then get on to those phases of our work in this area which are perhaps somewhat less known.

Stated in its simplest terms, the amendment establishes what we think, and I am sure you will agree, is a workable procedure whereby any substance, the intended use of which results, or may reasonably be expected to result, directly or indirectly, in its becoming a component of or otherwise affecting the characteristics of any food, must first have been found safe for that use. Obviously, the amendment says a great deal more than that, but rather than dwelling further on the amendment itself, I should like to discuss with you what we in the Food and Drug Administration have been doing in the way of

drafting regulations and preparing a listing of substances for which petitions need not be filed and how we propose to deal with petitions.

I am truly sorry that we were not able to have copies of the proposed regulations published and distributed sufficiently in advance of this meeting to have afforded you ample opportunity to have studied them and to have prepared questions regarding them to direct to us at this conference. Unfortunately, we were unable to accomplish this. However, on the theory of "better late than never," we have mimeographed those of the regulations that are ready for publication as proposals and have them available for prepublication distribution today. Actual publication in the *Federal Register* will probably occur early next week.

As most of you very well know, considerable interest has been expressed throughout the industry in what the regulations will say. We have had many welcome offers of assistance and worthwhile suggestions, all of which have been appreciated. They have also served to impress upon us the great desirability of consulting with you and your associates in endeavoring to draft the regulations in such fashion that they will accomplish the purposes of the amendment in a manner mutually satisfactory to government, industry and consumer. In order to get as wide comment as possible, we have decided to publish in the *Federal Register* as proposals those regulations which have been drafted thus far. Through this procedure any interested party who wishes to avail himself of the opportunity may be heard with respect to any of the proposals and may offer suggestions for changes, deletions or additions. While the proposals are in our judgment sound, or we of course would not be publishing them, we do not wish to imply either through the act of publication or anything that my colleagues or I may say at this conference that they are inviolate and would not be changed by us willingly if a suggested change has merit. The purpose of publication as a proposal rather than an order is expressly so that we may have the full benefit of your views and so that you will have full opportunity to express them. Copies of the proposals will be mailed to all persons who are on our list for receiving reprints of material which we cause to be published on food additives in the *Federal Register*. When you have had an opportunity to study your copy, you will quickly recognize that this first draft of regulations is not complete. Additional sections and proposed revisions will be published from time to time.

Without attempting to discuss in their entirety the proposed regulations prepared to date, there are a few portions in which, based on the tenor of our mail, we think you will be particularly interested. Perhaps the most interest has been expressed in the list of substances that are not considered subject to the clearance provisions of the amendment. Therefore, I'll discuss that first. As you know, substances generally recognized among appropriately qualified experts as being safe for their intended use in food are not food additives as defined by the statute. This recognition can be on the basis of a showing of safety through scientific procedures or, in the case of substances used in food prior to January 1, 1958, either through scientific procedures or experience based on common use in food. Note that the statute in the latter instance says "either . . . or." With this thought in mind we have proceeded to prepare a partial list of those substances in current use which we believe to be generally recognized as safe. We think it unnecessary and impracticable, if not impossible, to prepare a truly complete list. Many of the substances used in food —for example, water, sugar or salt—are so generally recognized as safe not only by qualified experts, but by consumers as well that their inclusion in a list of safe substances would serve no useful purpose. However, there are a great many substances which, while generally recognized as safe by the experts have not reached this rather exalted status in the eyes of consumers generally or many manufacturers as evidenced by our mail. These, then, are the materials and their accepted uses that we shall publish.

In preparing our list we debated on the best means for determining which of those substances that have common usage in food are generally recognized by qualified experts as safe despite the fact that they may not have been tested by scientific procedures. After much soul-searching, we concluded that this is not a problem which should be resolved by outright administrative fiat, but a decision in which the experts outside of the Food and Drug Administration should also be given a voice.

We decided that the most effective means for resolving the matter and polling expert opinion is to publish in the *Federal Register,* as part of our regulations, the partial list of those substances we believe to be generally recognized as safe by qualified experts. This listing will also be in the form of a proposal, and sufficient distribution will be given to it to assure that qualified experts have an opportunity to

see it and to make their comments. Based on the comment received, a final regulation will be issued, setting forth those substances and their conditions of use in food which experts generally accept as safe. The initial list will not be our complete proposal. It will be supplemented with additional materials soon. You will note, for example, the omission of flavoring substances. The Flavoring and Extract Manufacturers Association has agreed to furnish us with a list of such substances which they believe are in use and which are generally recognized by qualified experts as safe for such use. As soon as we receive this material we will publish a list of those substances with which we find ourselves in agreement. Again, this will be published as a proposal.

As in the case of the regulations generally, we will welcome your suggestions for changes and additions, and trust that they will be forthcoming. The list by no means represents our final judgment.

You will note that substances are listed generically—that is, all preservatives in one grouping, nutrients in another, etc., and that the list is divided into two major subdivisions. One gives substances generally recognized as safe in any food and in any quantity where propriety of use dictates and good manufacturing practices are observed. The other is of substances which are limited either in the amounts that may be used or the commodities in which they may be used, or both.

We have, in the past, sanctioned the use of new additives when it has been shown to our satisfaction through scientific procedures that their intended use in food is safe. Subsequently, the scientific studies made on many of these materials have been published and the substances have thus gained the status of general recognition among qualified experts as being safe. These materials will be included in the list I have just described.

There are some other substances, the use of which we have sanctioned but which have not been reported on in the literature. We have, at least tentatively, decided not to publish a list of these. Our reason is the fact that this data was furnished to us in confidence and does involve, to a degree, factors that may well be considered trade secrets. Obviously, any person to whom such prior sanction for the use of an additive has been given is well aware of that fact. If any persons have doubt in their minds about the status of products they are using and would care to write, we would be glad to re-express

our views. Likewise, if any other person sees that a substance is being used or would like to use it himself, but is not advised as to its status under the additives amendment, we will very gladly comment on its status for the specific use requested.

The regulations dealing with these lists will make it clear that the exemptions granted a listed substance or a prior sanction not listed is not a perpetual one. Whenever new evidence becomes available that shows that a substance is no longer entitled to such an exemption—for example, the coumarin instance of a few years back—it will be delisted. Delisting will be preceded by prior notice and a statement of the reason for such action.

We have been asked many times if we propose to prepare a "black list" of substances that may under no conditions be added to food. None has been prepared for publication nor is it our present intention to prepare such a list.

The proposed regulations will incorporate by reference substances approved for use in foods for which standards of identity have been promulgated.

We have been asked many times whether the regulations will spell out the type of scientific studies that must be made to determine the safety of an additive. The answer is "no." You will note from the regulations that, while we have touched on this subject, we have not attempted to spell out precisely what tests should be run to determine the suitability of an additive for a particular use. Instead we have said that unless evidence is available establishing that a different method and procedure will give *equally or more reliable* results, the Commission of Food and Drugs, in reaching a decision on any petition filed under the food-additives amendment, will apply the criterion for establishing safety for food additives that is outlined by the Food Protection Committee of the National Research Council in its publication entitled *Principles and Procedures for Evaluating the Safety of Intentional Chemical Additives in Foods.* It is not intended that the reference to this booklet should in any way stereotype the kind of investigations which will be conducted to establish the safety of food additives. We sincerely hope that the scientists, both in industry and government, will continue to strive to improve upon these methods. As new methods are developed that are equally as good as, or better than, those set forth in the booklet, they may be used. In order further to reduce doubt in this area, we have put a provision in

the regulations whereby, upon written request describing a proposed alternate method for determining safety of a food additive, the Commissioner will advise the inquirer whether in his opinion the method is a suitable one.

We have been asked many times whether we will make available for review by any interested person a petition filed in support of a proposed regulation on food additives. We do not believe that it would be equitable or in the best interests of all concerned for the Food and Drug Administration to make public, except as may be required pursuant to an administrative or judicial proceeding, any portion of a petition except that which is necessary for the publication of the proposed regulation and the order which the Commissioner will issue setting forth the conditions under which an additive may be used.

You will note that several of the regulations provide that you may write to the Commissioner for information on certain points—for example, the status of an additive under the amendment or the adequacy of a proposed method of scientific investigation. These are intended to facilitate compliance.

The regulations recognize the fact that there will be instances where a new-drug application will also involve a food-additive matter. For example, the use of a medicated feed intended for growth stimulation could well result in residue of the drug or one of its reduction products in edible animal by-products. The administration of the drug to the animal is a new-drug matter whereas the residue of drug in the edible animal by-product is a food-additive matter. Under the regulations we establish a procedure whereby a petitioner need file but a single petition, in this instance a new-drug application. When our new-drug branch receives an application which it finds will also involve a food-additive matter, it shall so notify the applicant and advise him that the matter is also being processed simultaneously under the food-additives amendment. Where both new-drug and food-additive questions are involved, a food additive regulation, where appropriate, will be published simultaneously with the effective date of a new-drug application.

Likewise, the regulations recognize the fact that many substances proposed for addition to standardized foods will also be subject to the food-additives amendment. Here, again, they provide for a procedure whereby the petitioner will submit a petition under the food-

standards provisions; where a food-additive matter is involved, the Commissioner will consider it automatically under both the food-additive section and the food-standards section of the law. Simultaneous regulations under both sections will issue.

We have been asked what the Food and Drug Administration would do in the event that it had before it a petition seeking the use of an additive in several foods when it found that it did not have sufficient information to warrant authorization for the use of the additive in all of the foods. While the regulations do not spell out what action we would take, nor do we believe it necessary that they do, we would take the position that obviously those uses for which adequate supporting data are not available would not be condoned by regulation. However, those uses for which adequate data are available would be authorized by regulation. In other words, we would simply try to separate the sheep from the goats and issue a regulation that could be justified by the data even though it does not encompass everything sought in the petition.

The actual processing of a petition by the Food and Drug Administration will be substantially similar to the procedure presently employed for dealing with new-drug applications and pesticide petitions. The regulations provide that within 15 days of receipt of a petition, the Commissioner will either file it or advise the petitioner why it is not suitable for filing. We think this a desirable mechanism because it does afford an opportunity for us to make a preliminary review of a petition; where it is obvious to us from this quick look that it is incomplete or deficient in some major respect, the formalities of proceeding through the *Federal Register* can be avoided.

Once the petition is filed, a notice of filing and the nature of the regulations sought is published in general terms in the *Federal Register*. We also proceed to consider the petition for the purpose of issuing an order relating to the conditions under which the additive may be used.

Without going into detail, let me say simply that where it does not appear from the data submitted that an order reasonably approximating that sought by the petitioner can be issued, the regulations provide a system whereby "the clock can be stopped" so that the time within which a petition must be considered will not expire before the petitioner can supply the additional data which may make the difference between getting a favorable or an unfavorable regulation. Fur-

thermore, we have included a regulation which will permit withdrawal of a petition without prejudice for future refiling.

These are perhaps the most significant aspects of the regulations proposed thus far. The regulations do follow rather closely existing regulations under the new-drug section of the law with respect to the preparation and submission of an application or petition and they follow quite closely the pesticide regulations with respect to the administrative and judicial review procedures. Since you are probably quite familiar with these, at least in a general sense, I shall not undertake to discuss them further at this time.

I would again like to call your attention to the fact that when you review these regulations and the proposed exemptions you will quickly recognize, as we do, that there are omissions. Whole new sections need to be added and, undoubtedly, revisions of the published material may be in order.

I wish to emphasize that the regulations that we are publishing are not necessarily our final judgment in each instance. They are simply what we presently believe appropriate. We have no doubt but that you will scrutinize them very carefully and give us your best-considered opinions on whatever changes or additions you think are appropriate. We shall look forward expectantly to your comments.

COLOR ADDITIVES

by

Winton B. Rankin

SYNTHETIC COLORS were used in food before the original Federal Food and Drugs Act was enacted more than 50 years ago. But they were known to have unusual potentiality for harm, so soon after the original pure food and drug law was passed, a special administrative procedure was developed by government and industry to safeguard colored food. A limited number of synthetic colors—called "coal-tar colors" because they were derived at that time from coal tar—were selected as safe for food use provided they were pure enough. These colors were listed in a government document called Food Inspection Decision No. 76, which was approved by the Secretaries of Agriculture, Treasury, and Commerce and Labor on June 18, 1907. The decision required each batch of permitted color

to be tested by competent experts and found free from harmful constituents. A few colors were added to this original list, but the tendency has been to restrict the number of synthetic colors allowed in food.

The present pure food law, enacted in 1938, reaffirmed the national policy of allowing synthetic colors in food subject to safeguards considered necessary to protect the public health and prevent deception of consumers. It gave legislative sanction to the established administrative practice of listing certain colors for use in food and requiring each batch of listed color to be tested by the Food and Drug Administration for purity before it could be marketed.

While the 1938 Congress recognized that most coal-tar colors are toxic, it thought that an adequate supply of harmless colors had been developed under the administrative practice of the preceding 30 years and, presumably, could continue to be developed as needed. Therefore, the Congress passed a law that requires a coal-tar color to be "harmless" before it may be placed on the approved list or certified for food use.

As we read the present law, it does not allow us to place a limit on how much coal-tar color may be used or to say that it can be used in one food and not in another. If we find that it is harmless, we can list it for use without limitation; if we find that it is capable of harm in some concentration, we must decline to list it at all.

Within the past few years, new scientific testing methods have shown that some of the coal-tar colors which were permitted in food as "harmless" are, in fact, capable of causing harm. Consequently, we have found it necessary to remove one red and two orange colors from the permitted list, and to propose that four yellow colors be removed. As these modern tests are applied to other food colors, additional ones may be found that will have to be delisted. They may show adverse effects when fed to laboratory animals at levels selected by our toxicologists as relevant for deciding whether the colors may be regarded as innocuous for unrestricted use in foods.

At our present rate of testing, it will be many years before we can complete the necessary safety studies on the various coal-tar colors already on the permitted list. During this time, colors which may prove to be harmful may continue to be used with full legal sanction. This poses a potential threat to the public health.

Further, there is a prospect of gradual removal of colors from the permitted list, with no indication that adequate substitutes will be developed which are suitable for acceptance on the list. On the contrary, there is every reason to believe that most new colors will be found to cause harm at low levels of feeding to test animals. In such case they will be unable to meet the stringent requirements of the present law that they be harmless for unrestricted use, although in the quantities needed to color particular foods they might be used safely under tolerance limitations. This poses a serious threat to established coloring practices in the food, drug and cosmetic fields.

Clearly, a re-evaluation of the national policy with respect to colors is required. Should it be by administrative, judicial or legislative action?

The Department of Health, Education, and Welfare may establish national policy in this field only within the guidelines set forth in the laws enacted by Congress. As indicated earlier, we believe the present law is quite clear and quite restrictive. We do not see any opportunity to take administrative action that will solve the problem.

Some wonder whether the new food-additives amendment could be interpreted as permitting us to establish safe levels for using coal-tar colors in foods even though they might show harm if used in other, higher amounts. It seems clear to us that Congress did not intend the new amendment to cover this field. The coal-tar color section of the food chapter of the law was not amended; it still requires a food color to be "harmless" before it may be listed for certification. The committee reports accompanying the amendment did not indicate any Congressional intent to have it replace the coal-tar color section.

Also, there was not one word of testimony in the six years that food-additive bills were being considered by Congressional committees to indicate this intent by the sponsors or supporters of any bill. On the contrary, the only witness who spoke on the subject—an industry representative—testified before a subcommittee of the House Committee on Interstate and Foreign Commerce of the Eighty-fifth Congress that the legislation should not cover coal-tar colors.

Some wonder whether the present law can be interpreted judicially to permit us to establish safe tolerances for coal-tar colors in food. A case which they hope may solve the dilemma was argued before the Supreme Court just a week ago (*Flemming v. Florida Citrus Exchange*, No. 27, October Term, 1958).

We do not see how the outcome of this case, whether it upholds the government's position or industry's, can solve adequately the broad questions before us.

The case before the Court is based on a provision of the food chapter of the Act—Section 406(a)—which deals with added poisonous and added deleterious substances and not harmless colors. It has no counterpart in the drug and cosmetic chapters. We were ordered to retain Red No. 3 on the approved list because of the special economic need for it in coloring oranges, a factor we believe irrelevant to the question of harmlessness.

Judicial interpretation of the law, even if it completely adopted industry's views, could hardly solve the public-health problem caused by the fact that at the present rate of testing the listed colors in our laboratories it will take over 20 years to determine whether all of the presently listed coal-tar colors are or are not harmless. Even at the end of that time we would not necessarily have the data upon which to decide what would be a safe level for those colors not found to be harmless. We are unable to justify such delay in securing sound answers to a public-health problem of this magnitude.

In this situation, a legislative re-examination of the entire subject of color additives for use in the food, drug, and cosmetic supplies of the country is indicated. We would welcome new and clear statutory directives as to national policy in this field and as to our duty in carrying out that policy.

Bills intended to remedy the situation were introduced before the last Congress, but there were no hearings. Probably, new bills will be proposed to the Eighty-sixth Congress when it meets next January.

Our Department is in accord with the view that we should be permitted to specify the conditions under which a color may be used when we accept it for use in food (or drugs or cosmetics). We think the basic provisions of the food-additives amendment can readily be used as a guide to an acceptable color-additives bill. In many respects the color-additives bill, sponsored by the coal-tar-color industry last year, would adequately meet the needs of government and the consumer. There are some respects in which we think the industry bill should be modified. These were stated in a letter our Department sent the chairman of the House Committee on Interstate and Foreign Commerce on June 27, 1958, about H. R. 8945. Copies of the letter are available upon request.

Some of the essential features we believe should be in a color-additive bill follow:

(1) The bill should apply to any color additive—not just "coal-tar colors."

(2) There should not be a blanket "grandfather clause" that would sanction continued use of a color simply because it was employed before the law is enacted. Continued use of the color should be based upon its safety, not upon the date it was first employed.

(3) Before a color additive may be marketed for use in food (or drugs or cosmetics), its suitability for such use should be established and it should be placed on a permitted list by the government.

(4) Where necessary, the purity and suitability of individual batches of permitted colors should be certified by the government before marketing, as coal-tar colors are now certified. But where certification is not necessary, we should have the authority to exempt a color from the certification requirements.

(5) The bill should expressly forbid the listing of a color for a use which will promote deception of the consumer or violate any provision of the Federal Food, Drug, and Cosmetic Act.

If such a law were enacted, this would require a material expansion of enforcement and educational activities on the colors to afford consumer protection equivalent to that available today.

Under the present certification system, the food and drug inspector need only determine that the colors being used in a food plant are certified, in order to assure himself that the law is being complied with. If known poisonous colors are used with tolerance limitations, he will have to determine not only whether the color is certified, but also the level at which it is employed—a determination which will have to be checked by periodic laboratory examination of samples of foods, drugs and cosmetics.

SCIENTIFIC DISCIPLINES USED IN EVALUATING FOOD-ADDITIVE PETITIONS

by

Robert S. Roe

THE PROGRAM this afternoon will deal with some of the scientific problems involved in evaluating food-additive petitions. A

rather wide spectrum of scientific disciplines will be drawn upon in this evaluation. My presentation will be brief, simply enumerating some of the scientific disciplines that are involved. We have present three panels of scientists who will present discussions of some of the techniques and problems in the scientific field. They will be prepared to discuss further various aspects of these problems in response to questions and inquiries that you may propound. Many of you may be familiar with statements that have been prepared and published by the Food Protection Committee of the Food and Nutrition Board of the National Research Council that deal with food additives and that enunciate certain principles and procedures for evaluating the safety of additives. I should like to refer to these statements because they provide a basis for our discussion that represents the views of the outstanding scientific authorities from industry, universities and government constituting the food-protection committee. In the booklet *Safe Use of Chemical Additives in Foods,* the committee makes this interesting statement:

> The distinction must be made between hazard and toxicity. Toxicity is the capacity of the substance to produce injury; hazard is the probability that injury will result from the use of the substance in the quantity and in the manner proposed. An estimate of the hazard in relation to any substance must be based upon knowledge of the toxicity and of the details of its use.

In this booklet, the committee further stated:

> Experimental studies of the physiological, pharmacological and biochemical behavior of a proposed additive, made in various species of laboratory animals and in limited number of humans, can reduce to a very low degree the uncertainty of safety of its general use.

In the booklet, *Principles and Procedures for Evaluating the Safety of Intentional Chemical Additives in Foods,* the committee has indicated four general principles which it thinks should be followed, and has discussed the evaluation of an additive in the light of these principles. I shall not enumerate them here nor will I review the committee's discussion of the basis of evaluation. I desire, however, to call attention to several points that are basic.

Before the safety of an additive can be evaluated it should be identifiable in chemical and physical terms and, if it is a mixture of compounds, the components should be adequately described. Reproducible composition should be assured by reference to appropriate physical and chemical constants. Adequately sensitive methods of analysis must be available. Sufficient information on the chemistry

of the additive must be known, to appraise its stability and its possible reactivity with components of the foods in which it may be used. Having defined or identified the additive, then, of course, the determination of its safety requires information on its toxicology. This involves investigation of the structural, biochemical and physiological changes it may induce in specific organs or body systems. Then, what effect, if any, does the additive have on the stability of nutrients in the foods in which it may appear or on the digestibility and utilization of the food?

These are some of the aspects that must be considered. It is apparent that the scientific disciplines involved in the evaluation of food additives include chemistry, biochemistry, physiology, pathology, pharmacology and nutrition. Other disciplines also may frequently be involved, such as bacteriology and medicine. In the case of well-known, long-used or well-defined chemical compounds, appraisals may be easy and relatively simple. In the case of many substances, however, adequate evaluation involves complex and difficult scientific problems.

It is our aim to sanction only those uses of additives that are without hazard to man. We do not think that it will be desirable or, indeed, possible to establish a rigid procedure applicable to all additives and all contemplated uses. For one thing, we do not wish to strait-jacket procedures or require meaningless procedures. For another, the scope of investigations and the types of tests necessary to determine safety will vary to some extent for the different types of additives and the varying purposes for which they are used. The investigations made must be adequate to satisfy our scientists as to the safety of the proposed uses. Actually, I think that it will turn out that the tests we will require are ones that you in industry have been applying for many years in the normal development of your products.

I shall call first on the panel concerned with chemical data on food additives and data on physical and technical effects. The members of this panel are Lowrie M. Beacham, Jr., food technologist and deputy director, Division of Food; Lessel L. Ramsey, chemist, Division of Food; J. William Cook, chemist, Division of Food. The chairman of the panel is Glenn G. Slocum, director, Division of Microbiology.

The next presentation will deal with pharmacological data on additives. The members of this panel are Bert J. Vos, M. D., pharmacologist and assistant director, Division of Pharmacology; O. Garth

Fitzhugh, pharmacologist and chief of Toxicity Branch, Division of Pharmacology; A. A. Nelson, M. D., pathologist and chief of Pathology Branch, Division of Pharmacology. The chairman is A. J. Lehman, M. D., director, Division of Pharmacology.

The third panel presentation will deal with nutritional and medical evaluations of additives. The panel members are A. H. Holland, Jr., M. D., medical director of the Bureau of Medicine; and O. L. Kline, acting director of the Division of Food. The chairman of the panel is Dr. Elmer M. Nelson, director, Division of Nutrition.

PHARMACOLOGICAL DATA NEEDED TO SHOW SAFETY OF FOOD ADDITIVES

by

O. G. Fitzhugh

ASSUMING that the chemistry of the proposed additive has been established, we proceed by animal experimentation to establish the safety of the required amount which will be consumed by man. It is not possible in a general outline to design a single program that will apply to each and every new food additive. Many times even after an experiment has begun, we observe changes in animals which cause us to change the approach.

In most instances we are dealing with a desired demonstration of safety for a small amount of a chemical which may be consumed by man for a long time—possibly a lifetime. Therefore, oral chronic-toxicity studies may be required. However, before such studies are started, other data are necessary. Results of both acute and subacute studies form a part of a petition for the use of a food additive.

Acute studies (determination of oral LD_{50}—that is, the amount which will kill 50 per cent of the animals) are done on at least three species of animals. If dogs are used as one of the species, an approximate LD_{50} only may be obtained.

Subacute studies (usually for 90 days) are conducted with two species of animals. Rats and dogs usually are used, and form a basis for the long-term studies. A limited number of animals are used for range finding, and then an experiment is set up with three dosage levels and the control. Blood-chemical and blood-cellular examinations and other clinical tests are made at regular intervals. In larger

animals, pretreatment examinations are made. Biochemical and special studies of various kinds, depending on the nature of the test substance, are done with the subacute animals (enzyme studies, nutritional and utilization studies, storage, metabolism, etc., are exceedingly useful in evaluating certain substances). At the termination of the experiment, gross observations are made on all animals, major organs weighed and tissues preserved for microscopic examination (reports on these tissues are part of the final evaluation). The techniques employed should determine the effects of the compound—both anatomical and functional. The lowest dosage level at which these effects occur during the 90 days should be determined.

The chronic study stems from the information gained in the subacute experiment, and has for its purpose the establishment of a safe tolerance for each food additive. In order to do this, there must be a "no effect" level (a level in which the treatment has caused no change in the animals) of the chemical on the experimental animals. On the basis of the "no effect" level, we can use an appropriate margin of safety (100-fold margin of safety for food additives). The following outline represents what is needed:

Animals.—Rats and dogs are used in most instances.

Test Groups.—Three test groups and one control group are used. There should be a test group which gives no effect either functional or anatomical; a second test group which produces marked effect, preferably causing some deaths within the first year of the experiment; and a third test group between the other two. Additional test groups will aid in evaluation of safety.

Time of Observation.—The test substance is given to both species for two years.

Clinical Laboratory and Biochemical Tests.—Blood and urine chemistry and blood-cellular examinations are standard tests for all experiments. Functional tests, such as of the effects on enzyme systems, are needed with certain compounds (for example, organic phosphates for cholinesterase effects). Absorption, excretion, storage and metabolism play an important role with many compounds. Especially is this true with drugs which may become part of the edible portion of food animals (some information for the use of such products may be derived from tests with laboratory animals; although complete information may require tests on the particular food animal).

In these cases we ask: (1) Is the compound stored in some edible tissue (fat, etc.)—either in its original form or in an altered form? If it is altered, what is this new substance and what is its chronic toxicity? (3) What, if any, is the significance of their relative proportions in storage if both are present? (4) How stable is the storage depot? (5) What is the time relationship of the build-up in the animal tissue (long-term use may change the type and place of storage)? (6) What is the excretion pattern—also, when and how is it excreted? (Is it in milk of cows, eggs of poultry, etc.?)

Metabolism studies aid vitally in evaluating safety of an additive. If a complex compound is converted on absorption from the gastrointestinal tract to a normal constituent of the body, it is a good indication that the body can handle a reasonable amount of the substance.

Gross Pathology.—All changes (growth, food intake, general appearance and behavior of animals, time of occurrence of any change, death, etc. of each animal) are recorded. At death or termination of experiment, gross examinations of all animals are made.

Organ Weights.—Weights of important organs (liver, kidney, spleen, heart, testes or ovaries, thyroid and adrenals) are recorded.

Microscopic Pathology.—Organs and tissues of all large animals and of a sufficient number of the rats on the various dosage levels to evaluate changes are examined, and results are recorded.

Other special studies to supplement the two-year studies are used, as required, in testing for the safety of various substances.

Our final objective is to establish a "no effect" level in two species of animals and an "effect" level (both a minimal effect level and a severely toxic effect level are desirable) in the test animals. Records of the observations on each individual animal and the statistical treatment of the data as a whole are needed to reach a conclusion. In the last analysis, the caliber of the scientist conducting the various experiments and making the evaluations determines to a large extent the nature and usefulness of the animal-toxicity tests.

INTRODUCTION OF PANEL ON CHEMICAL DATA ON FOOD ADDITIVES

by

Glenn G. Slocum

IT IS MY PRIVILEGE to serve as chairman of the panel assigned the subject of "Chemical Data on Food Additives."

The framework for our discussion derives from the specific requirements of the food-additives amendment to the Federal Food, Drug, and Cosmetic Act. Among other things, this amendment requires that petitions to establish safety of food additives shall contain:

(1) The name and all pertinent information concerning such food additive, including, where available, its chemical identity and composition.

(2) A description of practicable methods for determining the quantity of such additive in or on food, and any substance formed in or on food, because of its use.

(3) All relevant data bearing on the physical or other technical effect such additive is intended to produce, and the quantity of such additive required to produce such effect.

Other provisions of the amendment pertinent to this subject area will be discussed by the individual panel members.

Mr. Roe has pointed out the importance of certain essential chemical data to the assessment of the safety of food additives. We have on our panel today two scientists, Lessel L. Ramsey and J. W. Cook, chemists, Division of Food, Food and Drug Administration, who are well qualified to discuss the identity and determination of chemical additives in foods. To conserve time and facilitate presentation, this subject will be presented by Mr. Ramsey.

Mr. L. M. Beacham, deputy director of the Division of Food, will then discuss data relating to physical or other technical effects of proposed food additives, following which I will comment on "Data Relating to the Technical Effects of Preservatives."

CONSIDERATION OF DATA RELATING TO PHYSICAL OR OTHER TECHNICAL EFFECTS OF PROPOSED FOOD ADDITIVES

by

L. M. Beacham

THE food-additives amendment provides that the petition shall contain "all relevant data bearing on the physical or other technical effect such additive is intended to produce, and the quantity of such additive required to produce such effect." It also states that the Secretary of Health, Education, and Welfare shall not issue a regulation if a fair evaluation of the data before him:

. . . shows that the proposed use of the additive would promote the deception of the consumer in violation of this Act, or would otherwise result in adulteration or misbranding of food within the meaning of this Act.

The amendment further provides that if the Secretary decides that a tolerance is required, he:

. . . (A) shall not fix such tolerance limitation at a level higher than he finds to be reasonably required to accomplish the physical or other technical effect for which such additive is intended; and (B) shall not establish a regulation for such proposed use if he finds upon a fair evaluation of the data before him that such data do not establish that such use would accomplish the intended physical or other technical effect.

Food additives may be used for any of several purposes. These would include uses as antioxidants; as emulsifying agents; as stabilizers; as preservatives; to improve texture, appearance or flavor; and many other conceivable uses. To establish that the conditions of the Act are met will require the resources of experts in food technology and related disciplines. It will require that samples shall be carefully prepared of foods containing the proposed additive at several different levels of concentration, together with control samples identical in all respects except for the absence of the additive under investigation. Most of such data will be supplied by the petitioner; indeed, it is in large measure the type of information he will have had to acquire as a result of his own research into the satisfactory performance of the additive he has chosen to use. In order properly to evaluate the data it may in some cases be necessary for the trained personnel of the Food and Drug Administration to prepare, test and analyze samples of the type described above. Also, there will be many instances in which industry and government scientists, sitting around the table, can reach a better understanding in an hour than they could by exchanging numerous letters. We will work in close cooperation with the petitioner to develop the information needed, and to get a full understanding of his petition. In short, we will call upon the services of skilled chemists, bacteriologists, food technologists, and others to evaluate and determine the adequacy of the data submitted by the petitioner, to suggest areas that should be explored, and perhaps, sometimes, to develop original data of our own, in order to establish (1) that the proposed additive will in fact produce the effect claimed for it, (2) that accomplishing this effect will not result in deceiving the consumer or cause the food to be adulterated or misbranded under other provisions of the Act and (3) that no higher tolerance is established than is necessary.

No hard-and-fast rules can be projected as to how this is to be accomplished for each additive that may be proposed. The investigation required and the data that will be necessary will be dictated by the circumstances for each proposed additive and the effect sought for. Perhaps a description of one such hypothetical investigation will serve as a typical illustration, and Dr. Slocum is prepared to describe the type of investigation that might be required in the case of a food additive proposed for use as a preservative.

DATA RELATING TO THE TECHNICAL EFFECTS OF PRESERVATIVES

by

Glenn G. Slocum

AN important class of food additives includes those substances added to protect or preserve foods against the attack of micro-organisms. Substances effective for this purpose have been sought since the very beginning of organized society, and the search will continue as we seek ever to conserve food and to improve its distribution both within this country and throughout the world.

Food deterioration by micro-organisms is, of course, extremely complex and will vary with the nature and composition of the food; the groups or species of bacteria, yeasts or molds principally responsible for decomposition or fermentation; and the environment. Each of these three elements—food, micro-organisms and environment—represent variables which must be taken into account in measuring the technical effects of antimicrobial food additives.

In consideration of the development of evidence of satisfactory performance of a food or drug preservative, we are asked frequently to express an opinion as to the choice between controlled laboratory experiments and trials conducted under conditions of commercial production. Both provide useful and desirable, if not essential, information for proper appraisal of such technical effects.

The hypothetical investigation, suggested by Mr. Beacham, starts usually and preferably with laboratory research which permits control of the many variables and a study of their interactions with a minimum of materials. Time will permit only brief reference to some of the important points in such controlled laboratory research.

Micro-organisms.—The effect of various levels of the food additive is tested against the various groups or species of bacteria, yeasts or molds responsible for spoilage or deterioration of the food to be preserved. Since various strains of the same organism may vary widely in resistance to the food additives, tests should include strains isolated from several different sources.

In tests conducted with the food additive at different levels of concentration in laboratory media or in the food of known composition, it is important also to vary the number of micro-organisms added, including some with levels much higher than would be expected in the food produced under good commercial practice. This serves two purposes, both important under the food-additives amendment: (1) to define more sharply the critical concentration of the additive required for preservation and (2) to show whether the additive tends to mask the use of unfit raw materials or insanitary conditions of production.

Food.—It is essential that the food used in laboratory experiments be entirely representative of regular commercial production. Significant variations in composition may affect the results obtained. While the investigator has less latitude in varying the food composition without affecting its acceptability, it is possible that minor, acceptable changes may enhance the efficacy of the food additive, for example, it is well known that benzoic acid, sulfur dioxide and several other preservatives are more active in acid foods.

Environment.—The influence of environmental factors, such as temperature and humidity, representative of normal conditions and extremes likely to be encountered during storage and distribution of the food should also be studied.

The observed influence of the several variables on the effect of the food additive on micro-organisms as compared to control samples without the food additive serves to define rather sharply the efficacy of the additive and the amount required to produce the intended effect.

There is no substitute for trial under practical conditions of commercial production to translate laboratory findings into accomplished fact. Trials on extensive samples of commercial lots of the food without and with critical levels of the additives are needed to confirm and harden research findings or to indicate necessary adjustment to meet the vagaries of practical application. The scope of such tests will vary from case to case, but of a certainty will be substantially less

demanding than similar trials to establish technical effects without the laboratory research background.

As Mr. Beacham has suggested, the data required to support a petition for an additive intended to control micro-organisms in food is essentially that acquired by the petitioner in research to develop an additive of satisfactory performance.

CHEMICAL DATA REQUIRED TO SUPPORT USAGE OF FOOD ADDITIVES

by

L. L. Ramsey

AS HAS BEEN INDICATED by Mr. Roe, a petition for the use of a food additive must be supported by data fulfilling three basic requirements with respect to chemistry: (1) The additive must be identified; (2) the quantity of additive and its conversion products, if any, in the food must be known; and (3) a practicable method for determining the quantity of additive and its conversion products, if any, in the food must be furnished. This information is essential for the purpose of guiding the pharmacologist in his studies directed toward appraising the safety of the proposed usage.

If the additive consists of a single pure chemical compound, characterization in the usual manner is generally quite straightforward, there being well-established means of identifying and defining it by reference to appropriate physical, chemical and/or biological constants. However, many substances found useful in food are not single chemical entities. When they deviate relatively little from that status, they are said to be impure. As they deviate more substantially, they approach what is referred to as a mixture, the basic difference being one only of degree. Extending this trend, a point may be reached where the substance is no longer readily visualized as a mixture of individual entities, and practicality may demand that it be treated as a mixture of classes of entities.

Impurities, or coconstituents of a substance, may or may not be significant to appraisal of its safety; there is no way to tell until each has been identified and its amount determined with such delicacy and precision as its identity and other circumstances may dictate. Some of the more fruitful clues as to what needs to be known in this regard

are ordinarily gained from an understanding of how the substance is produced, what materials go into it, and in what proportions. In short, it may become essential that the manufacturing process be described, the detail necessary being directly related to the toxicity of the additive and to its proposed usage. In some instances, a description of the manufacturing process is actually required to identify the additive clearly.

The quantitative composition of the additive, including trace impurities, should be furnished. Complete chemical analyses of typical batches for the major components and for the impurities expected are necessary to demonstrate that the composition of the additive is reproducible from batch to batch and from one month's production to another. Incidentally, in reporting an analysis for an impurity, it is hardly adequate to state "none detected." In order to make the finding informative, the analytical method employed for determining the impurity should be described and its sensitivity given.

Specifications for the food additive proposed by the manufacturer should be furnished as a basis for establishing an acceptable standard of purity. Since it is usually impossible to eliminate all impurities from a food additive, it is a proper function of the specifications to establish the minimum content of the major component(s) and the maximum permissible levels of impurities. Controls employed by the manufacturer to assure that each batch of additive offered for food use meets the specifications should be described.

Having satisfactorily identified the additive, proposed standards of purity, and demonstrated that the production controls are adequate to assure a product meeting these standards, we must turn our attention to the second requirement of determining *what* is actually present in the food when it is ingested and *how much*. Such questions as the following must be answered: Is the additive stable or unstable in the food? Does it react with any food component and, if so, what products are formed? If it is a feed additive, is there a residue incurred by its usage in the production of meat, milk, or eggs and, if so, what is the identity of the residue? It would ordinarily serve little purpose to evaluate the safety of the original substance if, in the food man will consume, it has changed to something else. What it has become may or may not be more hazardous than the original. A serious obstacle to learning which, or to proceeding toward finding out how much is present, obviously exists until the transformation product is identified.

Therefore, prior to embarking on chronic-toxicity studies of a chemical additive, it is fundamental to ascertain whether it is the chemical *per se* or some transformation product which will be ingested under the conditions of the proposed usage. A favorite question of the pharmacologist for the chemist—and one for which the chemist may need a substantial amount of data—is: Was the substance fed to the animals in the chronic-toxicity studies identical in all respects with the substance which man will ingest under the proposed usage?

With regard to *how much*, the matter is relatively simple when a substance is added directly to a food in which it is stable, for a knowledge of how much is there is easily gained from knowing how much was put in. However, if the additive alters its identity in the food or is partially dissipated in the processing or manufacture, the development of adequate qualitative and quantitative methods may be a task of no mean order of magnitude.

This consideration brings us to the third chemical requirement of a petition, the analytical method. Generally speaking, it would be imprudent to contemplate the addition of any substance to food which for safety reasons must be limited in amount, unless there were available an analytical method of adequate sensitivity and reliability for its quantitative determination therein. Sensitivity required is normally related to the degree to which the substance must be limited. As a rule, we have considered a method inadequate unless it will detect as little as one tenth of the limited amount or tolerance and afford an analytical recovery within $\pm$ 10 per cent at the tolerance level. We deem some relaxation of this rule justified, and usually necessary, where the tolerance is less than 1 part per million. An analytical method submitted in support of a petition should be accompanied by validation data, that is, data showing blanks on untreated foods and recoveries of the substance added to the various foods at the proposed tolerance level.

The quantity of data to satisfy these three basic requirements, or the degree of assurance deemed necessary, will vary somewhat from one additive to another, depending primarily upon toxicity, but also upon usage level. For an additive containing a very toxic component as an impurity, we would need a higher order of assurance with respect to reproducibility of composition—more data—than for an additive containing no components of appreciable toxicity. Also, for an additive going into a basic food at a level of 0.5 per cent we would need

more assurance—again, more data—than for an additive of the same order of toxicity going into a minor food at a level of 0.001 per cent.

Food packaging materials present a problem of possible incidental additives in contrast to intentional additives. Use of a plastic film wrapper or container coating in contact with food may require a petition, depending on whether or not there occurs a transfer to the food of any components of the wrapper or coating, by reason of such contact. In seeking a solution to this problem we need, first, the complete quantitative composition of the film or coating, including the reproducibility of this composition and, second, data showing with the necessary degree of sensitivity and reliability the quantity of each component which may transfer to the food. With regard to this second requirement, we are interested in any transfer of the basic polymer itself as well as of monomer, low-molecular-weight polymers, plasticizers, stabilizers, catalyst residues, fillers, antioxidants, protective colloids, or other components of the film or coating.

A description of the manufacturing process is almost indispensable in evaluating the problem. Since a change in the percentage of one component of a plastic or in the manufacturing process, such as in the polymerization or, further, in the degree of resin cure, may have a marked effect on the chemical and physical properties of the plastic, we are constrained to recommend that each formulated packaging material be individually evaluated. If the composition, or the manufacturing, of a plastic film or coating is altered slightly, tests should be conducted to determine whether its potential for contaminating food has also been altered.

Ideally, the best procedure for determining whether any components of a plastic film or coating transfer to the food contacting it would be to package various foods in accordance with the proposed commercial practice, to hold or store at the highest temperature and for the longest period of time anticipated in actual usage, and then to analyze the foods for the packaging components. However, analytical methods are inadequate for analyses for most packaging components in foods at the high sensitivities required, which may be as great as 0.01 p. p. m. Therefore, to obviate analytical difficulties, simple solvents are used to simulate action of any food or beverage in assessing the likely degree of contamination.

Testing for extractability should simulate extreme conditions to which the packaging material may be subjected in use. Obviously,

there are wide variations in this regard, and no one set of test conditions can fit all cases with uniform propriety. After exposure of the film or coating to the test solvents for an appropriate period of time, the extracts must needs be analyzed for the components of the film or coating. However, before contemplating the quantitative determination of minor components, it is always advisable to compute how much food contamination they would represent if they were entirely extractable. Instances have been encountered where it could be thus established that ultimate potential for transfer into food would be of insignificant magnitude—and a testing job that could pose considerable difficulty thereby be avoided.

The research division of Continental Can Company has developed a method of testing extractability of can liner enamels which has been widely followed. Their brochure, *A Method for the Quantitative Determination of Can Enamel Extractables* (1953), details the procedure, test solvents, and conditions of test.

If the requirements which I have so briefly discussed appear to be rather formidable, let me hasten to assure you that whereas yesterday they might have been, today they most certainly are not, for today the analytical chemist has at his disposal a veritable arsenal of analytical weapons which he can bring to bear upon the chemical problems facing the proponent of a food additive. We suggest that you encourage him to draw upon this arsenal for the purpose of gauging the qualitative and quantitative aspects of the exposure of man to the proposed additive usage.

DISCUSSION OF NUTRITIONAL AND MEDICAL EVALUATION OF FOOD ADDITIVES

by

E. M. Nelson

OUR ACTIVITIES will be devoted largely to the study of methods to be used in testing for hazards in the use of food additives. Mr. Roe has told you that hazard has been defined as the probability that injury will result from the use of a substance in the quantity and in the manner proposed. The methods that have been in use during the past 20 years have served the purpose of revealing toxicity, and they will continue to do so. They have been revised and refined in certain details, but they are basically the same as when they were devised.

The growth test for demonstrating toxicity became possible when studies in nutrition had developed to the extent that it was possible to raise rats on diets the constituents of which were fairly well known. Since that time, there have been very important developments in the knowledge of intermediary metabolism of various nutrients. It seems possible that by systematic study of these various reactions we can learn where the abnormal attack on body metabolism begins and, thereby, devise methods that will supplement observations on the intact animal.

There have been a number of observations that indicate that existing hazards cannot necessarily be predicted on the basis of toxicity studies.

You are familiar with difficulties that have been encountered in the use of agene, trichloroethylene and ethylene oxide, the use of which will be discussed more in detail by O. L. Kline. A thorough knowledge of the chemical and physiological changes induced by the use of such food additives in processing will best enable one to predict what may happen in the use of other food additives. Following Dr. Kline's discussion of the nutritional aspects, W. H. Kessenich will discuss the medical aspects of this problem.

We have received relatively little assistance from academic institutions in the development of methods for these purposes. There seems to be more glory for those who make discoveries in other fields. We may have been negligent in not calling our problems to the attention of others in a way that would stimulate them to do more and also to seek the necessary support for such studies from you. We know that much progress can be made by full and free exchange of information with scientists in the industry, which will be helpful in solving our control problems and helpful to the industry in solving its own problems in the improvement of foods through the use of food additives.

NUTRITIONAL ASPECTS OF FOOD-ADDITIVE EVALUATION

by

O. L. Kline

FROM a nutritional standpoint we are concerned with two possible effects of food additives: the first, upon the nutritive value of the food itself and, the second, upon the nutritive state of the animal or person that consumes the additive. Tests for the first effect—that

upon the food itself—are straightforward and clear-cut. As for the second, demonstrations of changes in the physiological state of the animal, beyond those observed in the test for chronic toxicity, are difficult, and are best studied at the tissue level in animals subjected to a variety of dietary patterns.

As for the food itself, methods are well established for determining changes in vitamin content, alteration of amino-acid pattern, variation in protein quality, or qualitative changes in the fat or carbohydrate constituents of the food. With respect to the effects of chemical compounds upon a food ingredient, Mickelsen has coined the term "nutritional imprints." He and his group, and Engel and others, have studied the effects of compounds used in food processing that have a damaging effect upon the nutritionally important constituents of a food. For example, ethylene oxide, used as a fumigant, may destroy certain vitamins and amino acids in the food, yet the ethylene oxide itself is removed from the food after the fumigation process. Here a test of the safety of the ethylene oxide per se would have little meaning, but the nutritional imprint it has left, in terms of destroyed vitamins and amino acid, may be of significance. Another example is the use of trichloroethylene, used as a solvent in extraction of oil from soybeans. Cattle fed trichloroethylene-extracted soybeans developed a fatal disease, some symptoms of which were severe hemorrhage and aplastic anemia. The trichloroethylene itself was not the cause of the toxicity. It has been demonstrated that the solvent reacts with the amino acid cysteine to form S(dichloro-vinyl)l-cysteine, which is known to have fatal effects in cattle.

We are all familiar, of course, with the agene story. Nitrogen trichloride in the small amounts that were used for the bleaching of flour caused a change in the amino acid methionine, forming methionine sulfoxamine which was shown to produce neurological disturbances in dogs. The nitrogen trichloride itself was dissipated from the food, and furthermore was shown not to be the cause of the symptoms observed. This again emphasizes the need to examine the processed food for changes in nutritive value, as well as the safety of the food additive.

In the second category involving the physiological state of the animal, our thinking and our approaches depart from the conventional concepts of demonstrating safety and differ particularly with respect to a need for study with a variety of dietary patterns. Mr. Roe has pointed out that the food-protection committee publication has made a

distinction between toxicity and hazard. It states: "Toxicity is the capacity of the substance to produce injury. Hazard is the probability that injury will result from the use of the substance in the quantity and manner proposed." In evaluating hazard from a nutritional standpoint, we must learn the physiological effect of a given chemical compound. This leads us into the biochemical changes and metabolic alterations that may be so subtle as to avoid detection in the observation of the intact animal. More delicate and specific technics must be developed for this purpose. We are engaged in this kind of a research program.

Although we may draw upon the research findings of university and other research laboratories, the specific problems are ours (and yours). We must use great care to detect change in body composition —qualitative and quantitative changes in fat, protein or mineral composition of such tissues as heart, kidney, liver, muscle and blood; changes in kind or activity of specific enzyme systems; or alteration in digestibility of special nutrients or nonnutrients. When a deviation from the normal is found, we may need to examine the observed biochemical reaction under a variety of dietary conditions to determine its significance and to evaluate the probability of its constituting a hazard.

As an example of the problem, we have a wide distribution of products containing sorbitol and vitamin B_{12} following the discovery that sorbitol aids in the intestinal absorption of vitamin B_{12}. Without intent of sounding an alarm, we must ask and answer the obvious question: "What other compounds are better absorbed in the presence of sorbitol? Is the absorption of undesirable nonnutrient substances increased?" This can be answered by appropriate study.

We are particularly aware of a responsibility in initiating and conducting such studies as these when we consider that a food additive may be consumed as a part of the ordinary diet, with regularity, over a lifetime of an individual. It is very much in the public interest to pursue any and all approaches that will give us a better understanding of the relative hazard involved in the use of food additives. The results of our scientific investigations in this area have been, and will continue to be, promptly disseminated to our scientific colleagues in industry who have an interest. Only by close cooperation and frequent exchange of scientific approaches and research findings can we hope to meet our respective obligations.

CHALLENGES TO SCIENCE POSED BY THE FOOD-ADDITIVES AMENDMENT

by

Bernard L. Oser

THE REPORTS of the Congressional committees which accompanied the food-additives amendment of 1958 emphasized its twofold purpose, namely, to provide added protection to the health of consumers and to advance food technology by permitting the use of food additives at safe levels. While both of these objectives offer advantages, directly or indirectly, for the general public, recognition of the latter need is particularly welcomed by scientists concerned with problems of food production and distribution. The situation created by the existing law governing additions to food was untenable and unrealistic in the light of modern conditions. The Nation has been faced with a rapidly growing population and a diminishing labor supply especially on the farm and in the home. Mechanical and chemical tools have become increasingly available as a means of adjustment to these conditions. But with rare exceptions chemical substances have been regarded as poisons under the per-se doctrine in the 1938 Act, and their use as food additives could be justified only by necessity or unavoidability. That this law was not adapted to the changing needs became evident when numerous informal sanctions for the use of pesticides and other functional chemicals were granted and, subsequently, when the Miller Pesticide Amendment was enacted.

The food-additives amendment is now welcomed by food scientists as recognition of the needs of a dynamic, many-faceted industry. It cannot be denied that some have expressed fears that interpretation of portions of the statute, which gives wide discretionary power to the enforcement agency, may continue to hamper technological progress, but I, for one, choose to regard the stated Congressional objective of aiding technology as more than lip service.

Adoption of the amendment constituted in effect a *quid pro quo*, with the consumer benefiting directly or indirectly from both exchanges. In return for assuming the burden of pretesting for safety and of more rigid regulatory control, the food industry and associated industries have gained the opportunity to apply the fruits of research and development without coming up against the blank wall of proving

the necessity for that which is novel. The consumer gains through foods of improved nutritional, organoleptic and aesthetic quality—foods that are packed hygienically, that keep better, are easier to prepare, are available year-round and—all things considered—are more economical.

It is hardly necessary to tell this audience that having attained this vista of a land of Canaan, all its problems are far from solved. The long controversy over major procedural issues involved in the evolution of the amendment has drawn attention from certain matters of scientific substance embodied in it. The very definition of "food additive" which gives the new law its extremely broad scope contains the cardinal requirement that it must be:

> . . . generally recognized, among experts qualified by scientific training and experience to evaluate its safety, as having been adequately shown through scientific procedures . . . to be safe under the conditions of its intended use.

In the case of substances used prior to 1958, these experts may alternatively rely on "experience based on common use in food." Several witnesses at the Congressional hearings testified to the ambiguity of the concept of "general" recognition and the difficulty of establishing a consensus among experts in this rather diffuse area of specialization. There is as yet no doctorate degree nor board of certification for toxicologists engaged in safety evaluation. *Expertise* in these subjects has been acquired by pharmacologists, biochemists, nutritionists, pathologists and physicians. This does not mean that all practitioners of these disciplines are necessarily qualified to render judgments as to safety. The law does not imply, nor do I believe Food and Drug Administration scientists believe, that the only qualified experts are those in the employ of the government. The question then arises whether exemption from the requirements of the food-additives amendment can be expected when experts who are believed by industry to be qualified to make such judgments deem a substance to be safe under its conditions of use as a food additive.

At this point it should be stressed that differences of opinion are bound to occur among equally competent, conscientious and sincere scientists interpreting the same body of facts or experimental observations. The significance of small differences and the translation of findings in animals to man are but two examples of problems where subjective judgment can be applied to objective data. Individuals differ in their attitudes and approaches to such philosophical questions

as whether proof must be reasonable or absolute; whether "no quantity" should be regarded practically as mathematical zero or as a pharmacologically inconsequential and ignorable amount; whether weight should be given to hypothetical or presumptive risks as distinguished from known or experimentally demonstrable risks. To the scientist in the service of the regulated industries, the literal construction of laws offers little help in resolving such questions. It has been said:

> Each [legal] text was once drawn up by someone who presumably meant something by it; but once the document has left its author's hands, it is the document that matters, not any unexpressed meaning that still remains in the author's mind.

Hence, it surprises no one that collisions between experts occur. Scientists may have their own views of one another's competence and judgment, but there should not be—and I believe there never is—a question of their honesty and integrity, regardless of who employs them. One has frequently heard industry scientists say that however much they regretted certain adverse decisions of the Food and Drug Administration, they would decide similarly if they were in the driver's seat.

Nevertheless, it behooves all so-called experts to confess not only to their sterling qualities, but to their limitations as well. However trained, experienced and disciplined they may be in their respective fields of specialized knowledge, they consciously or subconsciously possess certain traits which they themselves must guard against. The expert must be careful not to sacrifice "the insight of common sense to the intensity of his experience"—to quote a prominent writer and critic. An overdeveloped caste spirit is frequently encountered among experts to the degree that they may become unwilling to accept views from outside their own disciplines or from groups within their own professional ranks. This lack of humility may manifest itself in ways which may cause one to question the reputed objectivity of scientists.

Nevertheless, while having respect for the opinions of others, the expert must have the courage of his convictions and must stand up for them against pressures from within and without his own ranks. Scientists should attempt to resolve their scientific differences among themselves rather than bring these differences to legal experts for settlement. To quote John L. Harvey, Deputy Commissioner of Food and Drugs:

> . . . the greatest possible use of the completely informal pre-hearing discussions, involved in the across-the-desk and around-the-table exchange among our

scientists and others qualified, no matter who pays their salaries, will lead to the best results with the minimum of protracted hearings and appellate litigation.

This is of particular importance in an area where decisions based on scientific judgment may conflict with commercial or administrative expediency. Experts should remember the dictum "To thine own self be true . . . and . . . thou canst not then be false to any man." In concluding this perhaps-presumptuous bit of preachment, I cannot refrain from quoting the critic who wrote that "a sense of proportion in the expert is the safeguard against bureaucracy."

It will be apparent from these remarks that I believe the food industry will regret the last-minute decision of Congress to withdraw from the Administration bill (H. R. 6747) the privilege afforded industry of referral of disputed scientific questions to *ad hoc* scientific committees. The law governing pesticide-residue tolerances provides for such reviews, and the procedure has been invoked several times since its enactment. The coming years will at least present an opportunity for a controlled test of the efficiency of this step in the appellate procedure.

Consultants to the food industry are besieged with requests for guidance, concerning technical matters under the food-additives amendment, which industry is reluctant to seek directly from the enforcement agency. This attitude is understandable notwithstanding the willingness of the Food and Drug Administration to cooperate in every way with the industries under its regulatory control. Some of the issues raised by speakers on this morning's program and in the anonymous questions submitted to the Administration's panel this afternoon will reveal the concern of industry scientists. Answers to these questions will in large measure reflect the policies designed to implement the language and purposes of the amendment.

However, lest they be overlooked, I should like to exercise the prerogative of the chair and cite some food-additives problems which present a real challenge to scientists and toxicologists in the service of the food industries.

In the definition of "food additive," the phrase "experience in common use" is employed as a criterion for exemption. Does this comprehend the natural presence of a substance in food or does it refer only to its use as in additive? If the former is correct, many substances—particularly in the category of flavoring ingredients—could be regarded as exempt under the definition. However, if the latter is

correct, it would become essential to distinguish an added substance from the same component present naturally—a task no chemist would welcome. The definition of a food additive also includes "any source of radiation" which affects the composition or characteristics of food. Will this be interpreted to include heat which, of course, is a form of radiation?

The amendment contemplates the exclusion of additives whose use would be deceptive to the consumer. Any additive which protects a food against the changes which normally occur with time—whether these be microbial spoilage, rancidity, discoloration, or others—can be considered to conceal the true age of the food. Are such uses to be regarded as deceptive?

The analytical chemist has an immediate concern with problems raised by the amendment. Will the regulations describing the conditions of use of an additive disclose its specifications in great detail or in general terms? If the composition of an additive were regarded as a trade secret, how would it be described in the regulations? Petitions for the use of food additives must include methods for their determination in foods. To what extent will this be necessary in the case of additives for which no tolerance limit is either requested or required? Should a company expend its scientific manpower to develop analytical methods under such circumstances?

If toxicological studies of a substance—95 per cent of which consists of known chemical entities, the remainder being of unknown composition—indicated it to be safe for use, would it be necessary to identify the unknown component or components and to isolate it for further toxicological investigation?

The food technologist will have special responsibilities under this amendment inasmuch as he will be required to submit acceptable data establishing the "physical or other technical effect" which the additive is intended to produce. But what if these effects are of an intangible nature, such as those based on subjective, sensory response? Will this require taste-panel or similar psychometric studies or will sales responses be considered to constitute a suitable index of the effectiveness claimed for an additive?

The various types of toxicological investigation necessary to establish safety under conditions of use are well known to scientists working in the field of safety evaluation. Nevertheless, certain questions arise in relation to the amendment. In view of the ever-present

complication of effecting the transition from animal experiments to safety under conditions of use by man, it is well to recall that safe limits are, at best, educated guesses. These estimates, however, can be made with a high degree of assurance that no harm will result from intake levels below a safe limit. Fortunately, man is endowed with highly efficient defense mechanisms by virtue of which he either excretes or detoxifies small amounts of ingested foreign substances. Were it not for these defenses, traces of toxic materials would tend to accumulate, with the result that human individuals would gradually change in composition with age by virtue of variations in dietary habits and in environmental exposure to toxic agents. Nevertheless, all toxicologists are not in agreement in respect to their conception of what the human organism should be expected to tolerate as the price of advancing civilization. Some are wondering whether it will be the policy of the Food and Drug Administration to use its authority liberally to establish maximum levels for food additives or whether this authority will be exercised only where there is substantial reason to regard a tolerance level as essential to protect public health. Will the Food and Drug Administration insist on an arbitrary hundredfold safety factor between maximum noneffective dosage in animals and the human dietary level or will other factors (the slope of the dose-response curve, the built-in limitations against excessive use, etc.) be taken into account?

The amendment defines "safe" as referring to the health of man or animal. Is the word "animal" construed here as embracing the entire zoological kingdom? What if an additive is found to be unsafe for frogs or chickens, but safe for the mammalian species employed in its evaluation?

Does the concept of safety exclude every possible pathological state or manifestation, such as allergic reactions? Only a limited degree of protection has been afforded hypersensitive consumers under the present law. Can it be assumed that this policy will not be changed?

These are but a few of the many critical and perplexing questions that have been tossed into the lap of the scientist. While some may appear to be of a legal nature, they have far-reaching implications for research and development in the fields of food technology and safety evaluation. Cooperation between industry and government scientists in resolving these issues is a consummation devoutly to be wished.

Reasonable and effective enforcement of the food-additives amendment will require both clarification on the part of the enforcement agency and understanding on the part of the regulated industries. It has been suggested that a series of FDA-sponsored conferences, each devoted to a special class of food additives or to special areas of technological or scientific interest, may be in order during the coming months, as a means of delineating the responsibilities of industry under this new amendment. The present conference is an encouraging augury to that end.

THE SCIENTIFIC SIGNIFICANCE OF THE AMENDMENT TO THE FOOD-MANUFACTURING INDUSTRY

by

Fredus N. Peters, Jr.

IT IS probably too early to state with any great assurance what the scientific significance of the recent amendment of the food law will be. Indeed, it may be several years before even a reasonably accurate assessment of its meaning can be made. We must wait for the unfolding of a pattern of human behavior which will determine the real significance of the amendment. The law is merely a collection of many words of no significance until translated into action by the Food and Drug Administration and by the food industry. Obviously, if the amendment produces no action on the part of either of these groups, it has no significance. This leads to the proposition that the food industry and the Food and Drug Administration have the power to make this amendment of great or little significance. The direction in which this power is applied will be determined largely by those who are here today.

In considering the most significant item in the amendment, some might choose the mandatory pretesting of new additives. From a scientific viewpoint, this is relatively unimportant, for it merely makes obligatory a process which heretofore has been practiced by the great majority of food and chemical manufacturers. However, from a public-relations standpoint, the mere existence of the amendment should be beneficial to the food industry. It must be admitted that our industry's public relations have suffered much in past years because irresponsible

writers have alarmed the public by emphasizing there was no legal requirement for pretesting of additives and inferring thereby that no testing at all was being done. Now this argument is no longer tenable, since all new additives will have to be shown to be safe for their intended use.

It may be that the filing of a petition will deter some few manufacturers from adding new ingredients which contribute no major benefits to the food in question but, even if this be true, it is of no great significance. Other points might be discussed, but the remainder of this paper will be devoted to a development which could be generated or accelerated by this amendment and which may be of great significance. But achievement of this degree of significance will depend upon our basic approach to the interpretation of the amendment.

Some have said: "The law is on the books—we have to live with it; it doesn't matter what we think of it." Certainly we have to live with it, but what we think about it can be the difference between ill-concealed toleration, with lack of progress, and optimistic acceptance, with accelerated development of improved foods. Personal opinion can make the difference between a tolerant, wise and enlightened administration of the law, protecting the best interests of the public as well as the food manufacturer, and narrow, legalistic, and unrealistic regulations which benefit no one.

The development of the present amendment has been proceeding for many years. Scores of bills in this field have been put into the legislative hopper in the past eight years. Possibly, some of our feeling toward the 1958 amendment is really not applicable to it at all, but is a carry-over of objections to bills previously considered and rejected. If this be true, now is the time to forget what has gone before and to appraise the 1958 amendment on its own merits. If the appraisal is conducted with a background of hope that the new powers given to the Food and Drug Administration can be used as a whip to force a recalcitrant industry into line and to prevent the use of all but a minimum of food additives, then some comfort for this type of philosophy can be found in the amendment. Regardless of our own beliefs, we must recognize there are some persons who honestly believe the use of any synthetic additive should be stopped. There are those who believe vitamin B_1 synthesized by nature is much better than thiamine produced in a chemical plant. There are some who profess to believe food manufacturers have no regard for the public health and that their sole

interest is in profits. These persons would appraise the new amendment and decide it is a step in what they conceive to be the right direction but that it is still too tolerant in that additives are permitted. It is conceivable that a person with this point of view could rise to a high post in the Food and Drug Administration. Under such an administration, the new amendment could be used to limit the introduction of new additives and to make the cost of testing for safety prohibitive.

On the other hand, if the administrator believes that the food industry is conscious of, and responsive to, demands of public health and nutrition, if he believes scientific knowledge should be applied to food manufacture and if he recognizes that absolute and universal safety can never be established for any additive, then his appraisal of this amendment, as well as his administration of its provisions, will differ greatly from those of the individual first described. It is evident, then, that the rate of scientific developments under the amendment will depend greatly upon the fundamental beliefs of the federal officials, for these beliefs will be reflected in their regulations and interpretations. These will determine, to a great extent, industry's response to the amendment. It was only yesterday that these first regulations were announced, and today they will be discussed and explained further. Undoubtedly, they will be modified many times within the next few years.

Having now indicated how an individual or group viewpoint can affect the interpretation of a law and its impact on industry, let us consider how an industry viewpoint can affect the significance of the 1958 amendment. It should be very evident that if the food industry is to gain anything from this amendment, it must wholeheartedly accept its provisions and emphasize those areas which have not heretofore been fully open for development—this is to say that food manufacturers should think of this amendment as being beneficial rather than as merely another statute to be observed.

All of us remember the rash of articles eight or more years ago deploring the use of chemicals in foods. The title of one article was "Poison On Your Pantry Shelf," and the statement was made that hundreds, or even thousands, of untested chemicals were being added regularly to foods and were endangering the health, if not the lives, of our children. In such an atmosphere, the word "chemical" in connection with foods was used almost as a synonym for adulteration, fraud, or even criminality. The belief was common that any addition

to natural foods should be viewed with suspicion. The more radical stated that any processed food was suspect. It required considerable courage for a manufacturer to proclaim publicly that he was deliberately adding a synthetic material to a food product. The food industry went on the defensive, and for some years food faddists and even some scientists who should have known better held the spotlight as the only true protectors of the public health. Some of them even accused the Food and Drug Administration of being in league with the large food and chemical manufacturers in the latter's alleged efforts to undermine public health. Although informed persons recognized that it would be necessary to use more and more additives as time progressed, there seemed to be no basis for educating the public to this fact.

The recent amendment and some events leading up to its adoption have changed the picture. Various persons in the Food and Drug division have stated publicly that additives are necessary for the preservation, maintenance or improvement of the Nation's food supply. A Congressional committee has reported that additives are often important and desirable, and the Congress, by creating the law, has endorsed the use of additives. A new era is here. For the first time, scientists, food manufacturers, the federal agency charged with responsibility of guarding the Nation's food supply against debasement, and the Congress have all endorsed a single proposition. These events have removed any legal or official stigma from the use of additives. The food industry is in a position to adopt all the scientific advances available for the development of more convenient, attractive and nutritious foods subject, under a wise administrator, only to reasonable rules assuring that no health hazards are introduced. This is of great scientific significance. The time has arrived when no apology need be made for the incorporation of additives. We can proceed to erase the stigma attached to "synthetic," "artificial" or "chemical."

In addition to this, the Commissioner of Food and Drugs has expressed interest that simplified nomenclature be adopted which will no longer frighten the public with such ingredient declarations as "contains butylated hydroxytoluene, butylated hydroxyanisole and propylgallate." The industry can abandon its defensive attitude and go on the offensive, confident of its application of scientific knowledge. Who knows—possibly the time will come that, aided by a wise administration of this amendment and increased research and development on the part of the food industry, the American housewife will prefer some

foods largely of synthetic origin. This has occurred in the field of wearing apparel. Why should it not be repeated in the field of foods? Obviously, this change in public attitude will not occur overnight and will require a great deal of cooperation between food manufacturers, chemical industry and the Food and Drug Administration. Great sums will have to be spent, and will be spent, on advertising, but now it can be constructive rather than phrased in an apologetic or defensive manner. I believe it possible that in 1965 we may look back and say that 1958 marked the beginning of an unprecedented expansion in food research and technology, brought about or encouraged by the 1958 food law amendment which gave the green light to food manufacturers to utilize all scientific aids compatible with preservation of public health and welfare. Should this be true, this would be the greatest scientific significance of the 1958 amendment.

SCIENTIFIC PROBLEMS UNDER THE FOOD-ADDITIVES AMENDMENT, ILLUSTRATED BY COLOR AND FLAVOR ADDITIVES

by

R. C. Sherwood

THE food-additives amendment of 1958—Public Law 85-929, passed by the Eighty-fifth Congress can be heralded as one of the giant steps in food legislation. Because of the widespread usage of food ingredients classed as food additives, it will have far-reaching effects.

When Congress assigned the name "food-additives amendment," it was a wise choice of terminology. This item may appear trivial to some, but I think it is important. For several years the additives to be regulated by the Federal Food, Drug, and Cosmetic Act have been branded "chemical additives," and the word "chemical" has been used unfairly by alarmists to create fear of many of our modern foods to which small amounts of harmless substances have been added. Consumers of food who have little knowledge about food technology should react more favorably to the term "food additives."

Undoubtedly, the enactment of this amendment is in the interest of consumers of food. Although the record of the food industry over the years has been excellent, respecting safety-in-use of food additives, better rules and regulations for pretesting eventually will benefit in-

dustry, government and the ultimate consumers of food. I say "eventually" because this amendment creates many problems, and much time will be required to work out these problems without undue hardship upon manufacturers and consumers. With wise and careful planning, and with thorough cooperation of industry and government, it should be possible to avoid depriving consumers of the great variety of foods to which they have become accustomed. I suspect that many people in industry are more concerned right now about the possible interruption of existing safe practices in usage of food additives than they are about pretesting new additives that may be developed in the future.

Despite the fact that a very important feature of the amendment relative to safety has been mentioned on many occasions, it would be an oversight if I omitted comment about it. I am referring to the virtual abandonment of the per-se doctrine which has long hampered both government and industry. Safety of food additives under conditions of use is the proper criterion, but unfortunately the original provisions of the Act did not permit evaluation on this basis in all situations.

The amendment contains general instructions for the Secretary to follow in evaluating safety of food additives, and it outlines the topics to be included in a petition for the issuance of a regulation prescribing the conditions under which such additive may be safely used. It is very gratifying to note that Congress did not fix the specific methods for determining safety. It is almost imperative to maintain a flexible approach to this important and continuously developing problem. New methods of tracing metabolic pathways, improved techniques in animal testing, consumption data, and considerations of history of use and of self-limiting characteristics should all receive appropriate attention when evaluating safety. The problems presented are so varied and complex that each case must be judged separately.

It seems clear from the reference to "experts qualified by scientific training and experience to evaluate safety" that Congress expects the Secretary to rely on experts both in and out of government.

Judging harmlessness of food additives under conditions of intended use is particularly important when one scrutinizes colors and flavors, the two classes of additives assigned to me as topics requiring special consideration. At this point, probably, I should state that I am not appearing as an official spokesman for either the color or the flavor

industry. My views are strictly my own, and not necessarily those of my company.

It is a well-known fact that certain colors, defined in the 1938 Act as coal-tar colors, must be batch-certified before they can be used in foods, drugs or cosmetics. Published regulations describe the procedures. I shall not recite these, but I must refer to certain details. In Section 406(b) of the 1938 Act, the Secretary of Health, Education, and Welfare is instructed to promulgate regulations providing for the listing of coal-tar colors which are harmless and suitable for use in food and for the certification of batches of such colors. Similar provisions in Sections 504 and 604 apply to drugs and to cosmetics, respectively.

Note the language chosen by Congress, "harmless and suitable for use in food." In recent years the Food and Drug Administration has interpreted this expression as being harmless under any and all conditions of use, whereas the original interpretation was harmless as used in foods. Testimony of an FDA pharmacologist in Congressional hearings prior to passage of the 1938 Act stressed safety of the certifiable colors under conditions of use. Application of the newer interpretation has resulted in the delisting of three colors, leaving 16 in the certifiable list of FD&C colors, except that one of the three (Red No. 32) was reinstated temporarily by Congressional act for use only on oranges.

Many in industry have disagreed with the newer and more restricted FDA interpretation of the word "harmless," and it has been suggested that the Secretary establish quantitative limitations for usage of certified colors in foods, if there is concern about safety at very high, abnormal levels. Such limitations stated on a color certificate would guide a user, and should provide a substantial bar to misuse. However, this view has not been accepted by FDA on the grounds that the Secretary lacked authority to establish limitations. Nevertheless, the color manufacturers three years ago voluntarily started labeling color packages "not to be used above 300 ppm in finished foods," believing that this statement would encourage carefully controlled usage.

After numerous conferences on this matter it was decided that the solution to the problem would be an amendment to the 1938 Act, authorizing the Secretary to establish quantitative limitations for color additives. Such a bill was prepared, and it was introduced in

the Eighty-fifth Congress by Congressman Curtis as H. R. 8945. As no action has been taken on the bill, a similar bill will be presented at the next session of Congress.

I have commented about H. R. 8945 and events leading to it because the need for such legislation still exists. The food-additives amendment does not directly affect the provisions in the 1938 Act relative to certification of colors.

With respect to pretesting of coal-tar color additives, the new amendment has nothing basically new. It has always been necessary to pretest a coal-tar color before it could become eligible for inclusion in the certifiable list. Pharmacological tests, chemical specifications, and description of method of analysis have been required since passage of the 1938 Act and issuance of color regulations as prescribed therein. In fact, pharmacological data demonstrating safety under conditions of use had been accumulated prior to passage of the 1938 Act. It can be said correctly that improvements in testing methods have been made since that time, but fundamentally the methods are the same, namely, animal feeding experiments plus observations during life, and autopsy thereafter. It would be a boon to all concerned if shorter methods for evaluating safety could be developed. In addition, there should be a reappraisal of some of the current thinking relative to magnitude of safety factors. Is there a sound scientific basis for applying the philosophy of hundredfold safety factor more or less indiscriminately? With particular reference to colors and flavors, do animal feeding levels 100 or 1,000 times intended use provide reliable indices to safety under conditions of intended use?

The passage of the new food-additives amendment does not eliminate the need for the proposed color-additive amendment, H. R. 8945. The current interpretation that colors must be harmless under any and all conditions of use will undoubtedly prevail until Congress specifically authorizes the Secretary of Health, Education, and Welfare to establish quantitative limitations for usage of colors whenever he deems this necessary. Briefly stated, the color-additive proposal would authorize:

> . . . regulations providing for the separate listing of color additives which are suitable for use in food and which are harmless under conditions of use specified in such listing. Such regulations may provide for maximum concentrations for the use of a color additive in or on any food, as necesary to protect the public health, and may provide for maximum concentrations of the same color additive in or on different foods, depending upon the relative importance of each color

additive to the several foods in which it is used and the relative significance of those several foods in the human diet.

It seems perfectly clear, however, that provisions in the new food-additives amendment which emphasize "conditions of intended use" establish a precedent that should help pave the way for passage of a color-additive amendment providing listing and certification of colors which are harmless under conditions of use.

Among other changes, the proposed color-additive amendment will remove the term "coal tar" from the Act. The term "coal tar," applied to certified colors, is misleading. Literally, many of the colors are now made from petroleum derivatives. The colors should not be described in terms of source, but as chemical entities. It is unscientific also to differentiate between a natural source and a synthetic source of the same substance in determining whether or not such substance should be exempt from regulatory rules. All color additives should be proven harmless under conditions of intended use and whenever a compound can be produced by chemical synthesis and its counterpart extracted from natural materials, the two sources of color should be treated the same under food-additive regulations; in fact, this basic principle is applicable regardless of whether the additive happens to be a color or some other type of food additive.

As mentioned earlier, pretesting of color additives is now, and has long been, an accepted requirement, and rightly so. But there is little incentive to undertake research for new colors when it is known that safety under conditions of intended use is not the criterion. Unless the proposed color-additive bill is enacted, the future prospects for new colors are indeed dim.

In addition to colors, I have been asked to discuss the impact of the food-additives amendment on flavors.

Flavoring substances are widely used in foods. Flavors come both from natural sources and from chemical synthesis. Some of the natural substances have been used for centuries. In general, flavors are used in extremely small percentages, and their usage is inherently self-limiting for obvious reasons. A grossly excessive addition of a flavoring substance would defeat the objective by causing unpalatability and possibly even rendering a food repulsive. Technically, all flavoring agents are additives, but each flavor or flavor component is a "food additive" as defined in the new amendment only if such substance is not generally recognized among experts, qualified by scientific

training and experience to evaluate its safety, as having been adequately shown either through scientific procedures or experience to be safe under the conditions of its intended use.

It is clearly apparent that this definition of the term "food additive" was chosen with great care, and with the realization of possible chaos if a host of substances commonly used and generally accepted as safe could not legally be classed as exempt. Probably it is generally known that officials of the Food and Drug Administration are currently engaged in the preparation of such an exempt list, and that industry is cooperating with government by supplying helpful information.

In the area of flavoring substances this task is singularly important, and it is complicated by the fact that flavors in common use contain such a large variety of components. It will not take long for flavor experts to prepare a list of such components and to classify them roughly as "widely used" or, on the contrary, "rarely used," but if consumption data are required, it will probably take many months to assemble.

In the meantime it is certainly desirable and necessary to establish without undue delay an exempt list of flavoring substances which have a long history of use without any indications of adverse effects.

As a basis for selecting each item for the exempt list there are several questions that we might ask ourselves.

(1) Is it a naturally occurring food material?

(2) Has the food substance been widely used with little or no refinement?

(3) Does the natural foodstuff contain distinctive flavor ingredients which have been extracted and used as concentrates?

(4) Are the extracts used to flavor foods at levels comparable to, or less than, those in nature?

(5) Is the flavor or flavor component a synthetic counterpart of a naturally occurring substance?

(6) Is the flavor or flavor component a compound obtained only by synthesis, and in common use for many years, without any indication of adverse effects?

Armed with answers to such questions, the safe flavoring agents eligible for exemption could be classed in four main groups: (1) spices, roots, barks, berries, etc. used as natural seasonings, (2) essential oils, oleoresins, natural extractives and distillates directly derived from

natural food sources, (3) chemical components identified in natural food substances, whether isolated from natural sources or produced synthetically and (4) flavor components produced synthetically, unknown in natural foodstuffs, commonly used for many years with no history of adverse effects.

Any flavor agent, or component, not falling logically into one of these four classes would seemingly require pharmacological evidence of safety for intended use and if adequate evidence were not available, it would automatically be classed administratively as a food-additive subject to the pretesting provisions of the new amendment.

Those persons who are familiar with the composition of flavoring agents are surely aware of the problems involved in preparation of a so-called "exempt list." This calls for exercise of good judgment on the part of both government and industry, and probably a substantial degree of tolerance on the part of "qualified experts" in the initial stages to avoid curtailment of flavoring practices which historically appear perfectly safe, but which lack directly supporting scientific evidence.

Another important problem, magnified, but not created, by the food-additives amendment pertains to methods for quantitative determination of food additives. In the portion of the amendment relative to petitions for the permissive use of new additives is a clause requiring description of practicable methods for determining the quantity of such additive in or on food, and any substance formed in or on food because of such use (Section 409(b)(2)(D)).

Obviously, this clause applies to all petitions for usage of new additives. It is not restricted to colors and flavors. Its impact elsewhere will be variable, and I shall not delve into that here. In the case of newly proposed colors of the types in the current certifiable list, the development of methods for determining the minute percentages in foods is not too imposing. Techniques are available.

When flavor components are considered, however, the situation is different and exceedingly difficult. Although there are methods for testing flavor components and specifications exist for purified compounds, for concentrates and for extracts, it may be unfeasible to devise methods for quantitative determination of the traces sometimes used in foods. A multiplicity of interfering substances which are normally present in the food may prevent accurate analyses. Can

paragraph (D), which requires description of a method, be interpreted with sufficient liberality to permit dependence upon formulations and qualitative tests for a new additive when no reliable quantitative method is available for determining traces in the finished foods? Of course, this question presupposes the submission of adequate safety data at levels of intended use.

Another point of great concern to flavor-additive manufacturers is publicity. Formulations for flavor additives are usually trade secrets. May a petitioner submit an application to FDA for a new flavoring composition with assurance that confidentialness will be preserved when a regulation is issued establishing the conditions of use? Can a regulation be issued without revelation of the exact quantitative intended usage of a flavor chemical? Is it not possible to publish a regulation providing *general* conditions for use as a "food flavor" or as a "food flavoring ingredient," provided the petition contains full information coupled with a request for secrecy? When regulations are written for usage of a food additive, will these regulations contain detailed specifications for the substance, standards of purity, etc., such as found in *United States Pharmacopoeia* monographs, and similar published listings?

An area of debate is the toxicological significance of minute traces of food additives. The new amendment provides, fortunately, an opportunity for the Secretary to make an administrative decision to exclude from the legal class of food additives a substance used in such minute amounts that qualified experts conclude it is safe for intended use because traces, if any, found in food are inconsequential in relation to public health. The subject of toxicological inconsequence has been adequately expounded by the Food Protection Committee in a statement released last July entitled "Insignificant Levels of Chemical Additives in Food." This can serve well as a guide for regulatory action. Such philosophy is particularly applicable in many situations involving flavors where it seems inconceivable that minute traces of flavor components could have any physiological significance.

Another item that appears to be a cause for concern is the clause in the amendment stating that no regulation shall issue if the proposed use of the additive would promote deception of the consumer, Section 409(c)(3)(B). Is this likely to be interpreted differently from previous regulations? Colors and flavors always improve appearance and

palatability of foods, thus improving their aesthetic value. Is there any likelihood that this may be construed as deception in the future?

Questions have arisen regarding the status of various agents, both required and optional, which are listed as ingredients in the definitions and standards of identity for foods. Will all of these substances automatically be included in the exempt list of substances safe under conditions of use? Also, will the same substances be exempt if they are used in similar nonstandardized foods? One example of this situation is enriched bread, for which there is a standard, and specialty bread, nonstandardized.

Labeling of foods to show the inclusion of coloring and flavoring agents has been considered adequate if terms such as "artificial color added" or "artificial flavor added" are used where appropriate. Surely there is no reason to expand these declarations. Reassurance would be helpful to industry.

These are only part of the new problems presented by enactment of the food-additives amendment. It is hoped—and I think we have a right to expect—that frank discussion of the issues plus cooperative efforts of experts in government and industry will promote effective application of the principles set forth in the food-additives amendment.

Laws can establish rules of order, but they do not automatically prevent abuses of safe, accepted practices adopted and employed by competent users of food additives. Ignorant or careless usage of safe additives by others can be avoided substantially by a combination of law enforcement and thorough education in the proper use of food additives. Both government and industry can contribute educationally.

SCIENTIFIC PROBLEMS UNDER THE AMENDMENT WITH RESPECT TO FOOD PACKAGING

by

John A. Zapp, Jr.

THE scientific problems raised under the Federal Food, Drug, and Cosmetic Act of 1938 and the food-additives amendment of 1958 with respect to food packaging are those concerned with proof of safety of the packaging material. I propose to discuss these problems, but I should like first to point out that there are two aspects to the problem of safety in food packaging and that perhaps the more im-

portant is the role of the container in keeping food safe rather than of rendering it unsafe.

Food is put into containers for several purposes: There is the matter of convenience. One has to carry the food home in some convenient container even if it is a plantain leaf or a gourd. There is the matter of attractiveness. Certain kinds of packages undoubtedly promote the sale of the product. For example, the mushroom industry, which has its center in the area where I live, is finding that modern transparent containers not only permit a longer useful shelf life of the product, but also have a much greater buyer appeal than the old chip baskets. There is the economy factor. Prepackaged foods give the consumer assurance that he is getting a standard quality and full measure for his money. Most important, however, is the matter of safety of the food, which must reach the consumer in usable condition. Dr. T. E. Friedemann of the United States Army Medical Nutrition Laboratory pointed out recently [1] that the average household, consisting of 3.42 persons, consumes about 70 pounds per week of processed foods and that the industry's most acute problem is preserving the acceptable qualities—keeping the food from spoiling. The first step in food processing is usually treatment by heat, by refrigeration, or by drying to stop or retard chemical reactions or bacterial growth. But even if food is made safe initially by such treatment, it must be protected by suitable containers from subsequent contamination during shipment and storage.

The importance of contamination of foods may be illustrated by reference to the annual reports of the Commissioner of Food and Drugs.[2] In 1956, food seized because it was filthy or decomposed totaled nearly 2,600 tons and accounted for 86 per cent of food seizures. In 1955, the corresponding figures were 3,909 tons or 88 per cent of the food seizures. In 1954, 2,544 tons of food was seized because it was filthy or decomposed, and this constituted 84 per cent of all food seizures.

Adequate processing and packaging could have prevented conditions such as these and undoubtedly are preventing immeasurably greater losses. Even a country like ours cannot afford to lose major amounts of food in the channels of distribution and, as our population

[1] "Medical and Public Health Aspects of Some Recent Developments in Nutrition and Food Technology," 17 *Federation Proceedings* 775 (1958).

[2] As quoted in V. A. Kleinfeld and C. W. Dunn, *Federal Food, Drug, and Cosmetic Act, Judicial and Administrative Record* 1953-1957 (Chicago, Commerce Clearing House, Inc., 1958).

continues to grow, food technology will be under an ever-increasing obligation to obtain the utmost yield from the available raw agricultural commodities. The positive contribution of food packaging to the safety of our food is real and important, and must not be overlooked when we consider the negative aspect, or possible harmful effect of the container on the food. The two should somehow be put into perspective and balanced against each other in the sense that we balance the benefits to be obtained through the use of automobiles against the accident toll.

Fortunately, at the present time we can afford to set very rigid standards for the safety of food-packaging materials as such. I say "afford" because we have a relative abundance of food and a relative abundance of packaging materials, and it is not too impractical at this time to sacrifice certain technologically valuable packaging materials in order to attain the desired degree of safety with respect to the packaging material as such.

What is the desired degree of safety? The Food, Drug, and Cosmetic Act of 1938 says [3] in Section 402(a)(6) that a food shall be deemed to be adulterated "if its container is composed in whole or in part of any poisonous or deleterious substance which may render the contents injurious to health." The food-additives amendment of 1958 does not modify the language of Section 402(a)(6) of the 1938 Act with respect to containers, but it does define the term "food additive" as:

> . . . any substance the intended use of which results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food (including any substance intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food . . .).

There is no doubt, therefore, that there is a legal requirement that food-packaging materials be safe and that unless there is a satisfactory demonstration of their safety, the packaged food may be deemed adulterated and liable to seizure. It may be pertinent at this time to refer to a statement by Drs. A. J. Lehman and W. I. Patterson [4] of the United States Food and Drug Administration in an article published in 1955 on basic considerations in determining safety of chemicals used in food-packaging materials. They state:

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[3] *Federal Food, Drug, and Cosmetic Act as Amended and General Regulations for Its Enforcement* (United States Government Printing Office, 1958).

[4] "F. & D. A. Acceptance Criteria—Basic Considerations in Determining Safety of Chemicals Used in Food-Packaging Materials," *Modern Packaging*, January, 1955.

The economic importance of these developments which effect better keeping qualities, add to the convenience, and reduce wastage cannot be overlooked, but must, in our opinion, take a secondary position to the legal requirement that our foods be safe.

To paraphrase this statement, poorer keeping qualities, less convenience and greater wastage of food is not too high a price to pay for the legal requirement that the food be safe. One cannot quarrel with this philosophy, but the key words are "legal requirement." At the moment these requirements are very rigid, and approved packaging materials must be safe beyond any probable—even possible—shadow of doubt. I believe that the day may come, however, when the "legal requirements" may recognize to a greater degree the positive contribution of the package to the safety of the food and take this into consideration in reaching an over-all judgment as to the safety of food-packaging materials.

There are various kinds of food-packaging materials in use today which come under the authority and control of the law. We will consider only primary packaging materials, that is, those which come in direct contact with the food. Prominent among these, of course, is metal, as typified by the various canned foods—yet in most cases the metal is coated with some sort of lacquer which forms a barrier between the food and the metal, and prevents corrosion. Glass is also used because of its transparency and chemical inertness, but glass containers must be sealed against oxygen and bacterial contamination, and this involves the problem of various sorts of gasket materials which contact the food. Paper and cardboard are still the major packaging materials for processed foods, but these materials are far more than just cellulose, since they are made tough, transparent, water-resistant, glossy or soft by the addition of various chemicals. Plastic materials are also common today, and we have both unmodified polymers like "Mylar" polyester resin and polymers which are modified by the addition of plasticizers, pigments, antioxidants, slip agents, coatings and the like. How can materials like these be shown to be safe?

There is one very simple approach to the problem of safety of food-packaging materials. If it can be demonstrated that a food-packaging material adds nothing whatever to the food packaged therein, there can obviously be no adulteration of the food and no problem with respect to the safety of the material for such use. The first approach, therefore, to the problem of the safety of a food-packaging

material is analytical. Does it or does it not contaminate food packaged therein? If the answer is "no," there is no problem.

As with many such propositions, however, the simplicity is somewhat deceptive. We are concerned with real foods and real containers, and the conclusive demonstration that pea soup or tomatoes or peanut butter, bread or milk has or has not picked up a tenth or a hundredth of a part per million or so of a contaminant during shelf life is somewhat of a challenge to the best of analysts. How long a time can elapse between packaging and consumption of a food? What temperature range can prevail over this time period? It is sufficient to say that the time can often be measured in years, and the temperature in the southern parts of the country may exceed 100° F. for substantial periods.

It is probably fair to say that analytical chemistry cannot cope at this time with all the problems of minute contamination of complex foodstuffs and that technology cannot afford to wait out long periods of shelf life before obtaining an answer.

Here, as in other branches of science, certain simplifying assumptions appear to be permissible. Any component of a food-packaging material capable of being dissolved by a food should be capable of being dissolved by simpler appropriate solvent systems such as water, salt solution, weak acid, weak base, syrups, or food fats, and such solutions present fewer problems to the analyst than milk, pickles or sardines. Also, it has long been recognized that most solutes dissolve more readily in hot than in cold solutions. Hence, a shorter extraction period at a higher temperature might be expected to yield as much in the way of extractable materials as a longer extraction at a lower temperature. Granting these assumptions, one must still make a choice of suitable solvent systems, suitable quantities of food-packaging material per unit volume of solvent, suitable extraction temperature and suitable extraction time. In addition, one must specify the desired degree of sensitivity of the analytical methods if one hopes to demonstrate that no material at all could be extracted by food under practical use conditions.

It is obvious that a great many combinations of the above variables could be specified and defended as permitting a practical solution to the problem at hand. The combination of greatest practical interest, however, is that recommended by the Food and Drug Administration,

since that agency must ultimately pass judgment and give or withhold approval of a proposed packaging material.

The latest published procedures recommended by the Food and Drug Administration for testing the extractability of food-packaging materials are contained in an article entitled "Food Packaging" by Dr. A. J. Lehman, Director of the Division of Pharmacology of the Food and Drug Administration. This article appeared in the October, 1956 issue of the *Quarterly Bulletin of the Association of Food and Drug Officials of the United States.* The procedures therein have since been expanded somewhat through verbal suggestions, and it is my understanding that an article will appear early in 1959, with further modifications.

The process of modification with respect to details of procedure is natural and inevitable. The procedures are empirical and must be adjusted on the basis of experience. I will briefly outline those currently recommended by the Food and Drug Administration, but with the reservation that they should not be considered either the best that can be found or the final recommendations of the FDA.

The first test is designed to demonstrate the "practical insolubility" of the resin itself. A one-milligram disc of the resin, as a film, is suspended in one liter of each of the following solvents: water; sodium chloride, 3 per cent in water; sodium bicarbonate, 3 per cent in water; acetic acid, 3 per cent in water; lactic acid, 3 per cent in water; sucrose, 20 per cent in water; citric acid, 1 per cent at pH of 3.5 containing 10 per cent sucrose by weight; lard or a vegetable oil. The container, with resin and solvent, is kept with constant agitation at a temperature of approximately 100° C. for one week. If, at the end of this period, some of the resin is still visible, it is concluded that the solubility of the resin is less than 1 p. p. m. in the given solvent system.

Alternatively, FDA has concluded that a resin is "practically insoluble" if its solubility is less than 2 p. p. m. when 300 mg. of the resin as a film of 400 square centimeters is exposed to 500 ml. of solvent at a temperature of 250° F. for two hours. Analytical methods sensitive to preferably better than 0.1 p. p. m. are required to demonstrate this degree of solubility.

Although these tests may suffice to demonstrate the practical insolubility of a resin, they tell nothing about the extractability of components of the resin. For this reason, FDA has suggested a further test in which 100 gms. of the resin as a one-mil film (that is,

30 to 40 square feet) is suspended with 100 ml. of solvent and maintained at 100° C. for one week. At the end of this period, the film is removed and the solvent analyzed for extracted materials. The amounts found are considered to represent maximum extraction for the given solvent system, and it is permissible to calculate how much would be extracted by a given volume of food surrounded by a given weight or area of the packaging material. A somewhat modified procedure can be used for food-can linings.

Generally, finite amounts of extractable materials will appear in the 100 gm., 100 ml., 100° C. test, and it would be strange if this were not so. By calculation, the amounts presumed to be extractable by food in an actual container will also be finite, however small. This leaves the very interesting and important question as to how much can be considered to be "practically zero." No hard-and-fast limits have been set, but present practice has been to ignore contaminations in the range of 0.01 to 0.1 p. p. m., depending upon the chemical nature of the extractable material.

Since the toxicity of chemicals varies widely from one compound to another, it does not seem entirely logical to agree to ignore an absolute amount of contamination—such as 0.01 or 0.1 p. p. m.—without reference to the toxicity of the contaminant. The real problem is that of defining inconsequential contamination, and it has been the experience of all practicing toxicologists that the toxic effects produced by a chemical at or above a given dose fade out and eventually disappear as the dose is reduced. To use an analogy, one aspirin tablet may cure a headache, but few people would expect a small fragment of an aspirin tablet to have any effect whatsoever.

The Food Protection Committee of the National Research Council has wrestled with the problem of inconsequential contamination, and a report entitled "Insignificant Levels of Chemical Additives in Food" has been published. This report recommends certain principles by which it should be possible to judge whether contamination of food by a given chemical may be so small as to be inconsequential in relation to public health, in which case "insofar as public health is concerned, regulatory action concerning it would be neither helpful nor necessary." [5] Whether the recommendations of this report will be accepted by FDA cannot be predicted at this time.

[5] 13 *Food Drug Cosmetic Law Journal* 477, 479 (July, 1958).

The Food Protection Committee is currently preparing a report on food-packaging materials, which will contain recommendations with respect to principles and methods to be used for the extraction by foods of components of packaging materials. These may or may not be identical with those currently recommended by FDA, but there is no compelling reason why they should be identical, for we are still in the stage of trial and error, and it would be unfortunate if our procedures became rigidly fixed by custom too soon.

I believe that we will witness a further evolution of procedures for testing the extractability of food-packaging materials and of criteria for determining whether a small finite contamination by one or more components of the material can be safely ignored. If, however, the outcome of some such set of procedures—either current or future—indicates that there is likely to be no contamination of any consequence of food in an actual container, then the legal requirement that the food be safe will, with respect to the packaging material, be met.

So far I have talked about the simple—perhaps deceptively simple—approach by which a food-packaging material might be demonstrated to be safe. But what happens if the tests—as they so often do—indicate that there is a likelihood of a finite contamination of food by one or more components which cannot, on a priori grounds, be excluded as inconsequential? In this case we would simply be dealing with unintentional food additives and, under the law, we could not use the packaging material until we were able to prove the safety of the unintentional additives under the proposed conditions of use. Proof of safety of food additives, however, is another story concerning which much has been said and written. I will not discuss it here except to express my personal opinion that there may be many routes to the desired end, and that no one route should be made mandatory. I say this because I believe that proof of safety will always be the result of thoughtful and considered research rather than of routine testing performed according to an established recipe.

In summary, food-packaging materials make a positive contribution to the safety of the food packaged within them, and this contribution is of great importance to the public health and economy. It will assume an even greater importance as our population grows larger and the relative abundance of raw agricultural commodities per capita decreases. It will always be required that the food-packaging material does not in itself make the food dangerous with respect to the public

health. The degree of safety required, however, is determined by law and custom. At the present time, both law and custom attach more importance to the requirement that a food-packaging material be safe than to its benefits in terms of better keeping qualities, reduced wastage and greater convenience.

The demonstration of safety can never be absolute, and there must always be some element of risk in the judgment that a food-packaging material or a food additive is safe. The element of risk which we are willing to accept today may differ from that which we may be willing to accept tomorrow in the light of conditions which may prevail tomorrow and do not prevail today.

There is one simple approach—in principle—to the demonstration of safety of a food-packaging material. It is the analytical approach whereby it may be shown that food is not contaminated by any consequential amount, with respect to the public health, of any component of the packaging material. This approach is not without its difficulties, but where there is no contamination of the food by any component of the packaging material there is no problem with respect to the safety of the packaging material for its intended use.

If the food is contaminated by components of the packaging material in amounts which cannot a priori be considered inconsequential with respect to the public health, then these components become unintentional food additives. The safety of their use, like that of all other food additives, must be demonstrated by techniques other than analytical.

COMMON LABEL NAMES FOR CHEMICAL FOOD ADDITIVES

by

Lloyd C. Miller

NAMING A CHEMICAL intended for use as a food additive is not the same as naming a baby. By way of pointing up the difference, imagine for a moment the problem that would exist if suddenly the parents of every new baby born this week in a city of the size of Milwaukee were required to find a name for their offspring that differed distinctly from that of every other person in the world, living or dead. Bear in mind further that the use of numbers or dangling letters would be banned and preferably the baby's name should be three or four syllables in length. This would be a grim out-

look indeed for those fond parents who had counted on having a "Junior" in the family. Fortunately, the problem does not exist. But the situation is all too real for the firm wishing to introduce a new product for use as a food additive within the framework of the 1958 food-additives amendment. In consequence, the food and chemical industries have a golden opportunity to make a sound attack on the problem of naming food additives. It is the purpose of these remarks to review briefly what approach has been made in other fields and to report progress on a course of action having a reasonable prospect of success.

Problem.—Substances intentionally added to processed foods range from very simple compounds, such as the inorganic salts, to the complex flavoring agents of unknown composition. However, regardless of the complexity, the new challenge is the immediate need for a means of referring to these additives in specific, convenient terms. It is imperative to have simple, distinctive names to identify the compounds in such a way as to facilitate our working with them and informing the consumer of their presence in the food he buys.

In addressing the American Chemical Society recently, Commissioner of Food and Drugs George P. Larrick expressed hope that this problem would be tackled forthrightly in the interest of fostering public confidence in foods. We may say, from our experience with drugs, that the industry will benefit greatly by agreeing upon the suitable names now in use and in selecting others where needed. The time to organize such a program is right now when the regulations are being formulated under the new amendment.

Guiding Principles of Nomenclature.—An analysis of the additives listed in the National Research Council report reveals that a substantial proportion of them are recognized in the current editions of either the *United States Pharmacopoeia* or the *National Formulary*. Thus, the group should present no problem on nomenclature, since few—if any—of their names ought to be changed. The colors and flavors provide their own peculiar nomenclature complexities but, otherwise, only three groups of additives appear to need immediate study. These are the antioxidants, the glycerides (including the natural fats) and the synthetic emulsifiers. Possibly, the inorganic phosphates need some sorting out but perhaps all that can be hoped for is that label readers become better chemists.

The first task is to reach agreement upon objectives. An example will illustrate some divergency in viewpoint here. Esters of para-hydroxybenzoic acid have been used as preservatives in both foods and drugs. In connection with the latter, two of them have been recognized in the *United States Pharmacopoeia* for several years under the simple titles Methylparaben and Propylparaben and, for drugs, these titles are used. However, for labels of foods, an FDA ruling of some years' standing directs that the full chemical names shall be used. This ruling reflects the view that consumers have been "sensitized" to the presence of benzoates in foods and thus expect to be informed when anything resembling benzoic acid is added. It is important to decide the extent to which such considerations shall prevail in setting aside short names that are already established.

The second task will be to decide upon the most suitable means of attaining the agreed-upon objectives. In deciding this, it may help to review what has been done here and abroad in closely related areas, namely, the selection of common names for drugs and the chemicals used to control pests.

Agencies Concerned with Selecting Names of Drugs.—The selection of common names for drugs has a long history in the United States. While the *United States Pharmacopoeia* has a clear claim to having been first concerned with the problem, actually the *United States Pharmacopoeia* long ago lost the initiative. The pharmacopoeia enters the picture as a rule only after the drugs it recognizes have become well established under common names.

Nearly 50 years ago, the American Medical Association took the lead in establishing common names for drugs through its council on pharmacy and chemistry. Under the "acceptance" program in effect until 1955, the council held virtually a veto power over naming of drugs—that is, until agreement was reached with the council on both the proprietary and nonproprietary names, the coveted AMA seal of acceptance was withheld. Without acceptance, no product could be advertised in any AMA publication. The approved nonproprietary names were called "generic names." This choice of terminology was unfortunate in view of the need for the term "generic" in its true sense. This is especially true for food additives where already several members of a class are in use. Admittedly, the term "nonproprietary name" is not nearly so convenient, but it does have the attractive attribute of specificity.

The AMA continues to render this invaluable service to the pharmaceutical industry, although the council now depends completely upon persuasion to get better compliance with what it regards as good nonproprietary nomenclature.

Our Federal Food, Drug, and Cosmetic Act calls for the "common or usual name" in labeling drugs. The Canadian Food and Drug Directorate interprets the term "common name" to mean the nonproprietary name. Neither the Food and Drug Administration nor the Food and Drug Directorate take part in selecting nonproprietary names beyond advising occasionally on whether a name used in proposed labeling is indeed a common one.

Through its trade-mark bureau, the Pharmaceutical Manufacturers Association provides a repository for trade-marks and nonproprietary names. Each week the bureau circulates a list of proposed names among the members of the association as a means of uncovering real or fancied conflict with established names. When a proposed name evokes no protest during the waiting period, it may proceed to the status of a trade-mark upon completing the registration formalities with the United States Patent Office. It would seem highly desirable to have the bureau circulate all names proposed for food additives.

In England, the British Pharmacopoeia Commission is the sole agency concerned with selecting names for drugs. The latter are selected upon request to the British Pharmacopoeia Commission in accordance with established principles, and are published as "British Approved Names."

France has a federal committee which selects names for drugs prior to permitting the latter to be sold. The Scandinavian countries have a joint international council for choosing what are known as the "N. F. N.," the abbreviation for the Danish equivalent of "Scandinavian Pharmacopoeia Names."

On a still broader international scale, the World Health Organization is instrumental in picking "Recommended International Nonproprietary Names" for drugs. These go through a process of proposal and final recommendation, after appropriate opportunity has been afforded for their review and possible protest on the part of those who feel that their trade-mark rights might be jeopardized. Some may

recall that the WHO program was subjected to considerable criticism in 1953. In consequence, minor but important changes were made, and it now appears that the procedure is working well from all standpoints except that of getting the names selected and published promptly enough to satisfy commercial interests.

Agencies Concerned with Common Names of Pesticides.—About two years ago, the American Standards Association inaugurated a service to the manufacturers of pesticides. A formal but fairly simple procedure is offered whereby to date 14 names for pest-control chemicals have been adopted and five are still "in the works." Under the ASA procedure, a "sponsor" submits a proposed common name for the pure compound involved. The sponsor, who is usually the manufacturer of the chemical concerned, informs the ASA of the proposed common name and provides a considerable amount of information on the chemical and physical properties of the compound, together with some data on its biological activity. In addition, the sponsor supplies the results of a search of the trade-mark register for names that are considered to be somewhat close to the proposed name. The sponsor agrees to allow unrestricted use of the proposed name if it is accepted as an ASA standard. Finally, he agrees to pay a substantial fee to reimburse the ASA for the expense that it incurs on this project. The British Standards Institution selects names for pest-control chemicals in Great Britain on a basis entirely comparable with the ASA procedure.

General Principles.—In attacking the problem of finding suitable and distinctive names for additives, certain general principles ought to be observed. Included among these are four that are ranked in the order of my opinion of their relative importance:

(1) Utility.—The pronunciation of the name should be both easy and obvious. The name recently adopted for iso-ascorbic acid, *erythorbic acid,* is so hard to pronounce that it rates rather low in utility. The name of the sodium salt, *sodium erythorbate,* presents even greater difficulty, at least without practice. Examples of names leaving room for doubt of their proper pronunciation are easy to find among our drugs. Such a case is the name Trilafon which has given enough trouble that the firm's advertisements now show the preferred phonetic spelling. A physician of my acquaintance looks forward to the introduction of the di-substituted congener under the name Dilafon, which he will pronounce "die laffin."

(2) Reasonable freedom of conflict with existing common names of foods or drugs.—This principle is important both to avoid confusion and to avoid trespass on trade-mark rights. We may be sure that the latter will generally be looked out for by those owning the trade-marks, but the public interest demands that, as the unexploited area of potentially useful combinations of syllables decreases, there must be a corresponding increase in the tolerance displayed by the owners of trade-marks. A German firm, for example, has filed a blanket protest with the WHO against the selection of any international nonproprietary name for a drug, beginning with the syllable "dex-"; this certainly appears to be an unjustified claim on a considerable portion of the public domain.

Finally, coined names should avoid conflict with systematic chemical names and also any possible suggestion of nonexistent relationships.

(3) Applicability.—The name should be suitable for both foods and drugs. Not only are good names too scarce to permit duplication, but it is a sad commentary on the level of public understanding if we must assume that people will generally be frightened to learn that foods may sometimes contain, quite safely, the same ingredients as drugs. To assume otherwise is to mar the image of perfect confidence we wish to create in the Food and Drug Administration as an agency entirely capable of safeguarding the quality of our foods and drugs.

(4) Brevity.—The time has passed when we can be too insistent upon short names, but certainly the first attempt should be in the range of three to four syllables rather than twice that length. The ridicule inspired by the discrepancy in length between the polysyllabic nonproprietary name and corresponding trade name for some of our drugs is, unfortunately, well deserved. While brevity must, perforce, rank a little lower than some other considerations, constant pressure must be exerted in the direction of achieving it by those who are expected to have regard for the public's interest.

By way of conclusion, substantial progress may be reported toward the establishment of a practical system of achieving the goals outlined above. Agreement has been reached upon approaching the ASA to undertake the project, and there is every prospect of complete success in this direction.

REPORT OF *AD HOC* COMMITTEE ON NOMENCLATURE OF FOOD ADDITIVES

THIS COMMITTEE was established by The Food Law Institute at the suggestion of Commissioner Larrick who, in an address before the American Bar Association, recommended that industry establish a representative committee for the purpose of adopting simple, common names to replace the long and complex chemical names of substances whose presence must be declared on food labels. It was decided that initially the committee be set up on an *ad hoc* basis in order that the problem first be defined following which a larger, more representative committee could be established to carry forward the objectives. The membership of the *ad hoc* committee and their respective affiliations follows: Dr. Leonard T. Capell, Chemical Abstracts, Ohio State University, Columbus 10, Ohio—Nomenclature Director and Executive Consultant; Dr. John S. Andrews, General Mills, Inc., 2010 East Hennepin Avenue, Minneapolis 13, Minnesota—Director of Food Research; Dr. Walter H. Hartung, Medical College of Virginia, Richmond 19, Virginia—Department of Chemistry and Pharmaceutical Chemistry; Dr. O. L. Kline, Food and Drug Administration, Department of Health, Education and Welfare, Washington 25, D. C.—Director of Research, Division of Nutrition; Dr. Lloyd C. Miller, Jr., 46 Park Avenue, New York 16, New York—Director of Revision, *U. S. Pharmacopoeia;* Mr. Kenneth A. Mulford, Atlas Powder Company, Wilmington 98, Delaware—Representing Manufacturing Chemists' Association; Mr. Harvey K. Murer, General Foods Corporation, 555 South Broadway, Tarrytown, New York—Director of Research; A. J. Nydick, Esq., 92 Liberty Street, New York 16, New York—Chemical Patents and Trademarks; Dr. Bernard L. Oser, Food and Drug Research Laboratories, Inc., Maurice Avenue at 58th Street, Maspeth 78, New York, New York—Chairman, representing Food Law Institute.

The *ad hoc* committee, through correspondence and an all-day conference (held at Food and Drug Research Laboratories, Inc., in New York City on November 10) reached the following conclusions:

1. Accepted nomenclature as used among scientists and experts must frequently and of necessity appear involved and cumbersome to the uninitiated. There is great need for the adoption of simple, easily

remembered names which can have informative value to the consumer in place of the incomprehensible, unrecognizable chemical names used on food labels, which, rather than educate, tend to cause doubts and fears.

2. This need also exists from the regulatory point of view by virtue of the present multiplicity and indefiniteness of chemical names used for label declaration purposes.

3. To correct this situation, some mechanism is needed whereby common names can be established for food additives on a basis which would be accceptable from both the technical and administrative point of view.

4. A similar situation, though for somewhat different reasons, has existed with respect to drugs and pesticides and agencies have been established to meet it in these fields.

5. It is recommended that the problem of common names of food additives can best be met by utilizing an existing facility, viz. a national organization whose scope, reputation and recognition would warrant general acceptance of its recommendations. Such an organization exists in the American Standards Association whose practice is to organize sectional committees of individuals representing all organizations having a legitimate interest in the problem at hand. A preliminary conference with a representative of the American Standards Association (affiliated with the development and application of the procedure "For the Acceptance of an American Standard Common Name for a Pest Control Chemical") has led the committee to conclude that the American Standards Association is a suitable medium through which common names can be developed for food additives.

6. The committee will endeavor to obtain the endorsement by the Food and Drug Administration, U. S. Department of Agriculture and the National Research Council of the sponsorship by the Food Law Institute of a request to the American Standards Association to convene for this purpose a conference of individuals representing organizations in the fields of chemical nomenclature, the chemical industries, food technology, the food industries, the regulatory agencies, the medical profession, pharmaceutical standards, food and trademark law, and consumer interests.

7. The objectives of this conference will be

(a) to consider the composition of a permanent sectional committee,

(b) to discuss the factors to be considered in establishing the rules of procedure for developing common names,

(c) to consider how best to defray the expenses of the committee's activities, that is whether by contributions from industry generally, by levying fees for consideration of and action upon proposed names (as is done in the case of pesticide chemicals) or by a combination of these means,

(d) to consider the means for implementing its recommendations.

FOOD-ADDITIVE LIAISON BETWEEN INDUSTRY AND GOVERNMENT THROUGH THE NATIONAL RESEARCH COUNCIL FOOD PROTECTION COMMITTEE

by

David B. Hand

Organization and Objectives of Food Protection Committee.—The Food Protection Committee was organized in 1950 for the purpose of advising both government and industry with respect to problems on the safety of food additives. The program of the committee is directed toward three general objectives: (1) to provide critical evaluation of information concerning the safety of food additives, (2) to stimulate the acquisition through research of information adequate to establish the safety of food additives and (3) to foster continued cooperation between industry and agencies of the public in insuring the wholesomeness and safety of the food supply.

The committee is a unit of the Food and Nutrition Board of the National Research Council. The work of the Food Protection Committee is carried on by four subcommittees—on toxicology, carcinogenesis, pesticides, and food technology.

Contact with industry is maintained through an annual meeting with a liaison panel. There are presently about 130 companies which are contributing financial support to the work of the Food Protection Committee and are participating in the meetings of the liaison panel. In addition to the industrial contributors, the liaison panel includes

trade associations and foundations, government agencies, and scientific and technical societies. An industry committee, which serves as a steering committee, is elected by the industry section of the liaison panel, and this smaller group meets several times a year with the Food Protection Committee. The industry committee was established to provide close liaison with industry and to enlist the support necessary for continuing the activities of the Food Protection Committee.

It can be seen that the organization of the Food Protection Committee provides frequent opportunities for informal discussion of the problems which are of interest to industry. Representatives of government also participate in the deliberations of the Food Protection Committee through membership on the subcommittees. Consultation with the industry committee and with the liaison panel is essential for a mutual understanding of the problems. However, the committee has reserved for itself the responsibility for all final judgments, conclusions, and preparation of reports. Public release of the committee's reports is subject only to the approval of the Food and Nutrition Board of the National Research Council.

Activities of Food Protection Committee.—The liaison between the Food Protection Committee and government and industry can best be illustrated by some examples of projects that have been undertaken. The subcommittee on toxicology has recently completed a review of the evidence for the safety of the polyoxyethylene stearates. For this study the unpublished data of both industry and government were made available. Mention should also be made of another publication of the committee enunciating principles and procedures for estimating the safety of intentional chemical additives in foods. The subcommittee on carcinogenesis was organized to investigate the possibility of dietary carcinogenesis from the standpoint of the use of chemical additives in foods. In a preliminary way the subcommittee has been occupied with definitions of terms and with an analysis of the problem to be studied. The report on this study, when it is completed, will undoubtedly stress the paucity of information and the need for research in the field of carcinogens. The subcommittee on pesticides has prepared a statement on the procedures necessary for evaluating the safety of pesticides for use in food production. This study also includes a description of the steps involved in developing pesticides. In cooperation with the food and chemical industries, the subcommittee on food technology has completed a survey of intentional additives in

foods and has prepared a list of approximately 500 of these additives, together with a statement of the functional benefits obtained from their use. More recently, the subcommittee has prepared a report of the components of food packaging materials. It is hoped that this report will be available by the end of the year. A closed symposium on food-packaging materials was held on the occasion of the annual meeting of the liaison panel in December, 1958.

The task of the Food Protection Committee has been modified by the enactment of the Miller bill regulating the use of pesticides. Under the Miller Amendment, the National Academy of Science is requested to suggest names for appointment to expert committees for the study of disputed questions connected with the assignment of tolerances to pesticides. This task of making nominations for expert committees has been assigned to the Food Protection Committee by the academy.

It is not yet clear to what extent the new food-additive amendment will affect the work of the Food Protection Committee, but it is certain that many new problems will develop.

Food Protection and Food Improvement.—Most of the problems concerned with intentional food additives have two important aspects. These are *food protection* and *food improvement.* The interests of the consumer need to be defended with respect to both of these aspects in such a way as to insure the continuation of progress as well as the maintenance of safety.

The responsibilities of government and industry differ with respect to the dual problems of food protection and food improvement. Of course, government and industry share a joint interest in both aspects, but it can be said that government has a primary responsibility for safety, and industry carries a primary responsibility for satisfying the consumer's need for improved products. More explicitly, the new food-additive amendment requires that industry obtain the evidence for the safety of a food additive and that government make the decision that this evidence is sufficient to establish safety. Since the enactment of the new food-additive amendment, industry still determines whether or not the effect of an additive is desirable to the consumer, but government must now decide whether the additive exerts the effect that is claimed for it. There are, thus, broad areas of interrelated responsibilities of both government and industry with respect to the safety of food additives and their functional benefits.

The interests of *food protection* and *food improvement* are sometimes mutually exclusive. Thus it is possible to emphasize safety so strongly that progress in new developments is retarded. The passage of the new food-additive amendment has made the problems with respect to food protection less critical. The food industry is justified at this time in seeking to set aside any unnecessary impediments to the development of new and improved foods.

Need for Expanded Research.—The new food-additive amendment has clarified the situation and solved many problems. But, obviously, some problems still remain. For example, the administration of the law requires certain judgments which, unfortunately, must be based on scientific facts that have not yet been discovered. A study of the wording of the law reveals some of the areas in which scientific research is urgently needed.

The need for more scientific knowledge can be illustrated in the case of provisions of the new food-additive amendment with respect to carcinogens. The law stipulates that no additive can be used in foods if it is found to induce cancer in man or animal either through ingestion or by some other appropriate test. This brings up a number of unanswered questions related to carcinogens. What is an appropriate test for cancer? What experimental animals are suitable for predicting the presence of cancer in man? Is there a relation between compounds which produce cancer after ingestion and those that produce skin cancer following subcutaneous injection? Is there a dosage response which will allow the estimation of a safe level for the use of substances which produce cancer in larger amounts?

Research should be expanded across the board in industrial and government laboratories and in universities. Each type of agency brings to its investigations a different point of view. Present indications are that people are genuinely aware of the needed expansion of research. The Food and Drug Administration has made recent moves to strengthen its research activities. There are a number of new industrial food-research laboratories which are either under construction or have been recently completed. There is also recognition by the United States Public Health Service of the need for expansion of its grant-in-aid program to provide for more work in food toxicology.

Expansion of research in the area of food toxicology is a long-term program. A limitation on the expansion of research in this field is the relatively small number of scientists with suitable training. There is

thus a need for the granting of educational fellowships in toxicology and for direct assistance to educational institutions in developing a training program.

Some of the research problems on which answers are urgently needed are of common interest to the entire food industry. For example, the development of improved techniques for toxicological tests and the extension of knowledge about the metabolic fate of additives are matters of wide interest to the food industry. Problems concerned with carcinogens have already been mentioned. The pursuance of these problems should not be left to individual companies, since this would certainly result in duplication of research. Some investigations might also be beyond the financial resources of individual companies.

There is a clear need for industry-wide cooperation in the support of scientific research. At the present time the industry committee of the liaison panel is the only organization that represents all segments of industry that are concerned with food additives. It would seem appropriate that the industry committee add the encouragement of research to the scope of its activities. This might be accomplished through granting of funds to universities and other research laboratories. Such grants could be administered by the Food Protection Committee if this proved to be desirable.

The industry committee occupies a unique position which is not filled by any trade association. Its representation covers not only the food industry but also chemical and pharmaceutical companies manufacturing food additives. It is safe to predict that the importance of the contributions that the industry committee is making will increase as the years go by and that the number of companies that are associated with this work will also greatly increase.

Need for Encouragement of Food Improvement.—There is an ever-present risk that too many controls will stifle progress. The new food-additive amendment has added a number of new regulations to the controls under which industry must operate. It would be worth while to re-examine the situation to see if any unnecessary legal impediments exist that might retard technological developments. One possibility has been mentioned which is worthy of careful consideration. In the interest of encouraging the continued improvement of foods and the development of new foods, it might be advantageous to simplify the standards of identity of foods that are promulgated

under the 1938 Federal Food, Drug, and Cosmetic Act. These standards protect the consumer's health as well as his pocketbook in three principal ways: (1) by requiring minimum amounts of economically significant ingredients, (2) by limiting the ingredients to those that have been proven to be safe and (3) by controlling the addition of vitamins.

With the passage of the new food-additive amendment, it is no longer necessary to rely on the Standards of Identity to insure the safety of foods. The purpose of the standards might thus be simplified at the present time and possibly restricted to questions of economic and nutritional importance. It is obvious that any unnecessary details on a standard of identity limits the flexibility of the manufacturer in improving the food.

It should be emphasized that there are some qualities of foods which the consumer is able to judge for himself. These are flavor, texture, appearance, and convenience for use. However, the consumer is not able to make his own decisions with respect to the nutritional value and healthfulness of a food.

One important benefit of the present standards of identity which should be retained is the control of the addition of vitamins to foods. It would not be in the interests of either the producer or the consumer if competition led to the addition of unnecessary vitamins to a large variety of foods.

In conclusion I would like to express optimism about the food-additive situation. The American public has good cause to be confident in the adequacy and safety of its food supply. Although the last 10 years have been disturbed by controversy and confusion, the dust has now settled and we can expect the next decade to be one of orderly progress in both the protection and the improvement of foods.

Beginning on the next page are the following related items: a list of chemicals, approved under the Federal Meat Inspection Act before September 6, 1958, which are exempted from the 1958 food-additives amendment; a list of acceptable materials for plastics intended for contact with federally inspected meat products; and the text of the proposed definitions and procedural and interpretative regulations with respect to food additives, as published in the *Federal Register* for December 9, 1958.

LIST OF CHEMICALS APPROVED UNDER FEDERAL MEAT INSPECTION ACT BEFORE SEPTEMBER 6, 1958, WHICH ARE EXEMPTED FROM 1958 FOOD ADDITIVES AMENDMENT OF FEDERAL FOOD, DRUG, AND COSMETIC ACT

UNITED STATES DEPARTMENT OF AGRICULTURE

Agricultural Research Service
Meat Inspection Division
Washington 25, D. C.

ZYLY-
MID-57-27
November 8, 1957

TO: Inspectors in Charge of Meat Inspection

FROM: R. M. Mehurin, Chief, Chemical Control Section

SUBJECT: Permitted Chemical Additives

Additive	*Reference*	*Purpose*	*Products*	*Amount*
Acetic acid	Reg. 18.7(i)	Refining	Rendered fats	Sufficient for purpose
Amines, filming	Correspondence	Volatile boiler additive to retard corrosion in pipes	Steam	See chemical names
Anti-foam A (methyl polysilicone)	Correspondence	To retard foaming	Soup	10 ppm
Antioxidants (oxygen interceptors)	Reg. 16.13(e); 18.7(d); 17.9(d)	To retard rancidity development	Lard and shortening	0.01% singly; 0.02% combinations
Ascorbic acid	Reg. 18.7(s); 28.3(b)(7)	Accelerate color fixing in curing	Cured cuts; cured comminuted product	7½ ozs. to 100 gals. pickle; ¾ oz. to 100 lbs. meat
Bacterial starter; lactic acid starter culture	Reg. 18.7(p) Memo. 234	To develop flavor	Dry sausage; pork roll	0.5%
Benzoate, sodium; benzoic acid	Reg. 28.1(a)(3)(ii), (b)(1)(v)	To retard flavor reversion	Oleomargarine	0.1%
BHA (butylated hydroxyanisole)	Reg. 17.9(d) 18.7(d)(5);	Antioxidant: To retard rancidity development	Lard and shortening	0.01%
	Reg. 18.7(t) 16.13(e)	Antioxidant: To retard rancidity development	Unsmoked dry sausage	0.003%

Additive	*Reference*	*Purpose*	*Products*	*Amount*
BHT (butylated hydroxytoluene)	Reg. 18.7(d)(6); 17.9(d)	Antioxidant: To retard rancidity development	Lard and shortening	0.01%
Bicarbonate of soda	Reg. 18.7(l); Correspondence	To neutralize excess acidity; cleaning vegts.	Rendered fats; tomato soup; beans, etc.	Sufficient for purpose
Borax	Reg. 17.9; 18.8	Preservative	Export	Sufficient for purpose
Bromelin	Correspondence	Same use as papain		
Carbon (purified charcoal)	Reg. 18.7(i)	Refining	Rendered fat	Sufficient for purpose
Carbon dioxide gas	Correspondence	Immobilizing	Hogs	Sufficient for purpose
Caseinate, sodium	Manual 18.28	Binder and extender	Imitation sausage; nonspecific loaves; soups; stews; etc.	Sufficient for purpose
Caustic soda (sodium hydroxide)	Reg. 18.7(i)(j)	Refining; denuding	Fats; tripe	Sufficient for purpose
Cellulose gum (carboxymethyl cellulose)	Correspondence	Extender, stabilizer	Baked pies, etc.	Sufficient for purpose
Citric acid	Reg. 18.7(d)(9)	Synergist: To increase effectiveness of antioxidants	Lard and shortening	0.01%
	Reg. 18.6(t)	Synergist: To increase effectiveness of antioxidants	Unsmoked dry sausage	0.01%
	Reg. 28.1(a)(3)(viii), (b)(1)(viii)	To protect flavor	Oleomargarine	Sufficient for purpose
	Correspondence	Flavoring	Chili con carne	Sufficient for purpose
Citric acid and sodium citrate	Reg. 18.7(o)	Prevent coagulation	Beef blood	0.2%
Coloring material, vegetable, and synthetic	Reg. 28.1(a)(3)(i), (b)(1)(iv); 18.7(m); (CFR Amendment 57-29); 17.9(a)(b); 16.7(a); 16.13(d)	To color casings, rendered fat, marking ink, etc.	Sausage casings; oleomargarine; shortening; branding ink	Sufficient for purpose

Additive	*Reference*	*Purpose*	*Products*	*Amount*
Corn syrup	Reg. 18.7(b)(q); Memo. 243	Flavor; cure	Cured product; hamburger	2.5%
Corn syrup dried	Reg. 18.7(b)(q); Memo. 243	Flavor; cure	Cured product; hamburger	2.0%
Cyclamate, sodium	Memo. 249	Sweetener	Bacon	0.15%
Cyclohexylamine	Correspondence	To retard corrosion	Boiler water	10 ppm from approved feeder
Dextrose	Reg. 18.7(b); 28.2(a)(4); Memo. 215	Flavor; cure; seasoning	Sausage, ham, etc.	Sufficient for purpose
Diacetyl	Reg. 28.1(a)(3)(iv), (b)(1)(vii)	Flavor	Oleomargarine	Sufficient for purpose
Diatomaceous earth	Reg. 18.7(i)	Refining	Rendered fats	Sufficient for purpose
Dry ice (carbon dioxide-solid)	Memo. 239	Cooling	Chopping of meat; packaging of product	Sufficient for purpose
Enzymes, proteolytic	See papain, bromelin, ficin			
Ficin	Correspondence	Same use as papain		
Fullers earth	Reg. 18.7(i)	Refining	Rendered fats	Sufficient for purpose
Glycerol (glycerine)	Reg. 18.6(a)(5) Correspondence	Inhibit drying; manufacture of mono- & diglycerides	Seasonings, curing mixes	Sufficient for purpose
Glycerol lactopalmitate, etc.	Correspondence	A type of mono- & diglycerides	Shortening	Sufficient for purpose
Gums, vegetable (tragacanth, karaya, etc.)	Correspondence	Emulsifying agent; binder	Spice emulsion; egg roll, breading mix	Sufficient for purpose
Hydrogen peroxide	Reg. 18.7(j)	Bleach	Tripe	Sufficient for purpose
Hydrolyzed plant protein	Reg. 28.2(b)(7) Manual 18.52 to 18.56	Flavor	Various	Sufficient for purpose
Isoascorbic acid	Reg. 18.7(s); 28.3(b)(7)	Accelerate color fixing in curing	Cured cuts; cured comminuted product	7½ ozs. to 100 gals. pickle; ¾ oz. to 100 lbs. meat
Isopropyl citrates	Reg. 28.1(a)(3)(ix), (b)(1)(ix)	To protect flavor	Oleomargarine	0.02%

Additive	*Reference*	*Purpose*	*Products*	*Amount*
Lecithin	Reg. 18.7(d) (4); Correspondence	To retard rancidity development; emulsifier	Lard and shortening	Sufficient for purpose
	Reg. 28.1(a)(9)	Emulsifier	Oleomargarine	0.5%
Lignin	Correspondence	Loosen scale	Steam boilers	Sufficient for purpose
Lime	Reg. 18.7(j)	Denude	Tripe	Sufficient for purpose
Malt syrup	Correspondence	Flavor; cure	Cured product	2.5%
Mono- and diglycerides	Reg. 17.8(c) (43); 18.7(c); 28.1(a)(9)	Emulsifiers	Lard, shortening; oleomargarine	Sufficient for purpose; 0.5% in oleomargarine
Monoisopropyl citrate	Reg. 18.7(d) (9); 28.1(a) (3)(ix), (b) (1)(ix)	To increase effectiveness of antioxidants	Lard, shortening; oleomargarine	0.01% in lard & shortening; 0.02% in oleomargarine
Monosodium glutamate	Reg. 28.2(b) (6); Manual 18.52 to 18.56	Flavor	Various	Sufficient for purpose
Morpholine	Correspondence	To retard corrosion	Boiler water	10 ppm from approved feeder
Nickel	Reg. 18.7(i)	Catalyst	Hydrogenated fats	Sufficient for purpose
Nitrate of soda or potassium	Reg. 18.7(k)	Source of nitrite	Cured products	See sodium or potassium nitrate
Nitrite of soda or potassium	Reg. 18.7(k)	Fix color	Cured products	See sodium or potassium nitrite
Nitrogen	Correspondence	Exclude oxygen	Sealed products	Sufficient for purpose
Nordihydroguaiaretic acid (NDGA)	Reg. 18.7(d)(2)	Antioxidant: To retard rancidity development	Lard and shortening	0.01%
Octadecylamine	Correspondence	Boiler additive to retard corrosion in steam pipes	Steam	2.5 ppm in condensed steam (analysis required)
Oxygen interceptor	Reg. 16.13(e); 17.9(d); 18.7(d)	See antioxidants		
Papain	Reg. 17.8(c) (56); Memo. 226	Soften tissue	Frozen cuts	Sufficient for purpose

Additive	*Reference*	*Purpose*	*Products*	*Amount*
Phosphates: disodium; sodium hexameta-; tripoly-; sodium pyro-; sodium acid pyrophosphate	Reg. 18.7(r); 18.7(t); 28.3(b)(6)	Decrease amount of cooked-out juices	Ham, pork shoulder picnic; canned chopped ham	5.0% in pumping pickle; 0.5% in canned chopped ham
Phosphate, sodium hexameta-	Correspondence	Retard scale formation in pipes	Potable water supply	10 ppm from approved feeder
Phosphate, trisodium	Reg. 18.7(j)	Denuder	Tripe	Sufficient for purpose
Phosphoric acid	Reg. 18.7(d)(9)	Synergist: To increase effectiveness of antioxidants	Lard and shortening	0.01%
Propyl gallate	Reg. 18.7(d)(7)	Antioxidant: To retard rancidity development	Lard and shortening	0.01%
Resin guaiac	Reg. 18.7(d)(1)	Antioxidant: To retard rancidity development	Lard and shortening	0.1%
Silica gel	Correspondence	Anti-caking agent	Curing mixes, etc.	0.5%
Sodium ascorbate; sodium isoascorbate	Reg. 18.7(s); 28.3(b)(7); Memo. 217, Supl. 1 & 2	Accelerate color fixing in curing	Cured cuts; cured comminuted product	7½ ozs. to 100 gals. pickle; ⅞ oz. to 100 lbs. meat; 10% soln. to surface of cured product prior to packaging
Sodium bicarbonate	See bicarbonate of soda			
Sodium carbonate	Reg. 18.7(i); 18.7(j)	Refining; denuding	Fats; tripe	Sufficient for purpose
Sodium caseinate	Manual 18.28	Binder and extender	Imitation sausage; non-specific loaves; soups; stews; etc.	Sufficient for purpose
Sodium hydroxide (caustic soda)	Reg. 18.7(j)	Denuder	Tripe	Sufficient for purpose

Additive	*Reference*	*Purpose*	*Products*	*Amount*
Sodium metasilicate	Reg. 18.7(j)	Denuder	Tripe	Sufficient for purpose
Sodium or potassium nitrate	Reg. 18.7(k)	Source of nitrite	Cured products	7 lbs. to 100 gals. pickle; 3½ ozs. to 100 lbs. meat (dry cure); 2¾ ozs. to 100 lbs. chopped meat
Sodium or potassium nitrite	Reg. 18.7(k)	Color fixing	Cured products	200 ppm (02%) in product; 2 lbs. to 100 gals. pickle; 1 oz. to 100 lbs. meat (dry cure); ¼ oz. to 100 lbs. chopped meat
Sodium sulfoacetate derivatives of mono- and diglycerides	Reg. 28.1(a)(9)	Emulsifier	Oleomargarine	0.5%
Sorbitol	Correspondence	Retard drying	Seasonings	Sufficient for purpose
Starter distillate	Reg. 28.1(a)(3)(iv), (b)(1)(vii)	Flavor	Oleomargarine	Sufficient for purpose
Stearyl citrate	Reg. 28.1(a)(3)(x), (b)(1)(x)	To protect flavor	Oleomargarine	0.15%
Sugars, approved (sucrose and dextrose)	Reg. 18.7(b); 28.2(a)(4); Memo. 215	Flavoring; curing; seasoning	Sausage, ham, miscellaneous	Sufficient for purpose
Sulphites with strong alkali	Correspondence	Retard corrosion	Boiler water	Sufficient for purpose
Tannic acid	Reg. 18.7(i); Correspondence	Refining; loosen scale	Rendered fats; boiler water	Sufficient for purpose
Tocopherols	Reg. 18.7(d)(3)	Antioxidant: To retard rancidity development	Lard and shortening	0.03%

Additive	*Reference*	*Purpose*	*Products*	*Amount*
Trisodium phosphate	Reg. 18.7(j)	Denuder	Tripe	Sufficient for purpose

This memorandum supersedes "Meat Inspection Division Memorandum No. 57-3, dated February 25, 1957.

R. M. Mehurin
[Signature]

ACCEPTABLE MATERIALS FOR PLASTICS, UNITED STATES DEPARTMENT OF AGRICULTURE, MEAT INSPECTION DIVISION, JANUARY, 1958

SYNTHETIC RESINS, PLASTICIZERS, STABILIZERS, DRIERS, DRYING OILS, COLORANTS AND RELEASE AGENTS APPROVED FOR USE IN RUBBER OR SYNTHETIC RESIN PLASTICS INTENDED FOR CONTACT WITH FEDERALLY INSPECTED MEAT FOOD PRODUCT

Resins

A. Can enamels

The classes of resins that have been met with most frequently are:

Bisphenol-epichlorhydrin
Bisphenol-epichlorhydrinesters
Epoxy ester
Bisphenol-epichlorhydrin-vinyl
Certain modified phenols
Certain modified vinyls
Oleoresins
Alkyl oleoresinous
Polyester
Alkyl ester

The basic types of resins may be listed as follows:

Fossil resins, specifically gilsonite, and natural East Indian and Congo resins
Bisphenol-formaldehyde
Certain substituted phenol formaldehydes
Phenol formaldehyde
Urea formaldehyde
Bisphenol-epichlorhydrin
Bisphenol-epichlorhydrin esters
Maleic anhydride resin ester
Esterified Congo resin
Esterified resin
Melamine-formaldehyde
Polyvinyl chloride and acetate
Cellulose acetate butyrate
Polystyrene
Polyvinyl butyral
Polyethylene
Petroleum hydrocarbon

B. Films for wrapping foods

The acceptable resins for wrapping foods are:

Condensate of dimethyl terephthalate and ethylene glycol
Resins from high and low viscosity polyvinyl alcohol for fatty foods only
Polyvinyl chloride
Polyvinyl acetate
Polyvinyl chloride-acetate
Vinylidine chloride
Polystyrene
Polyethylene of the high and low pressure type
Cellulose acetate
Regenerated cellulose
Butadiene-scrylonitrile synthetic rubber

Methyl and ethyl acrylate
Ethyl cellulose
Rubber hydrochloride
Polyester resin—ethylene terephthalate and ethylene isophthalate
Butadiene acrylonitrile-styrene copolymer
Butadiene-styrene copolymer
Terephthalic acid-ethylene glycol copolymer

C. Grease-proofing and wet-strength resins for paper wraps
Polymer of 2-chloro-butadiene
Polymer of melamine-formaldehyde
Polymer of urea-formaldehyde
Polymer of dimethyl-polysiloxane of 350 centistokes viscosity
Copolymer of styrene and isobutylene (for foods of high water content only)

Plasticizers
Acetyl tributyl citrate
Acetyl triethyl citrate
Butyl stearate
Butyl phthalyl butyl glycollate
p-Tertiary butyl phenyl salicylate
Dibutyl sebacate
Di-iso butyl adipate
Di-2-ethylhexyl phthalate (for foods of high water content only)
Di-iso-octyl phthalate (for food of high water content only)
Diethyl phthalate
2-Ethylhexyl diphenyl phosphate
Ethyl phthalyl ethyl glycollate
Glyceryl monooleate
Glycerin triaceate
Monisopropyl citrate
Paraplex G-60
Paraplex G-62
Stearyl citrate
Triethyl citrate
3-(2-Xenoxyl)-1,2-epoxypropane

Stabilizers
Aluminum monostearate
Ammonium citrate
Ammonium potassium phosphate
Calcium acetate
Calcium ethyl acetoacetate acetate
Calcium carbonate
Calcium glycerophosphate
Mono-, di- and tricalcium phosphate
Calcium oleate
Calcium ricinoleate
Calcium stearate
Magnesium glycerophosphate
Magnesium stearate
Mono-, di- and trimagnesium phosphate
Potassium citrate
Disodium hydrogen phosphate
Sodium citrate
Sodium pyrophosphate
Sodium tetrapyrophosphate
Tin stearate
Inorganic salts of copper-manganese, and zinc, zinc stearate and zinc resinate, are acceptable if the leaching of the metal contributes less than 50 parts per million to the food.

Driers
Cobalt caprylate, linoleate, naphthenate, and tallate
Iron caprylate, linoleate, naphthenate, and tallate
Manganese caprylate, linoleate, naphthenate, and tallate

Drying Oils
Chinawood oil
Dehydrated caster oil
Linseed oil
Tall oil

Colorants (Pigments)
Carbon black
Oxides of iron
Titanium dioxide (*National Formulary* grade)
Ultramarine blue

Release Agents
Acrowax C
DC Fluid 200 of 60,000 centistokes viscosity
Methyl polysiloxane of 350 centistokes viscosity

Microcrystalline wax
Linoleic acid amide
Oleic acid amide
Palmitic acid amide
Stearic acid amide
Polyethylene glycol 400
Polyethylene glycol 1500
Polyethylene glycol 4000
Polytetrafluoroethylene

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE FOOD AND DRUG ADMINISTRATION (21 CFR PART 121)

FOOD ADDITIVES

PROPOSED DEFINITIONS AND PROCEDURAL AND INTERPRETATIVE REGULATIONS

[*Federal Register*, December 9, 1958, pages 9511-9517]

The Commissioner of Food and Drugs, in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (secs. 201, 402, 409, 701; 72 Stat. 1784, 1785 et seq.; 52 Stat. 1055, as amended, 70 Stat. 919, 72 Stat. 948; 21 U. S. C. 321, 342, 348, 371) and pursuant to authority delegated to him by the Secretary of Health, Education, and Welfare, proposes the promulgation of the following regulations with respect to food additives, and hereby offers an opportunity to all interested persons to present their views in writing to the Hearing Clerk, Department of Health, Education, and Welfare, 330 Independence Avenue S. W., Washington 25, D. C., within 30 days from the date of publication of this notice in the FEDERAL REGISTER. Comments may be accompanied by a memorandum or brief, and it is requested that all comments be submitted in quintuplicate.

PART 121—FOOD ADDITIVES

SUBPART A—DEFINITIONS AND PROCEDURAL AND INTERPRETATIVE REGULATIONS

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SUBPART B—EXEMPTION OF CERTAIN FOOD ADDITIVES FROM THE REQUIREMENT OF TOLERANCES

Sec.

121.100 Substances that are generally recognized as safe.

SUBPART A—DEFINITIONS AND PROCEDURAL AND INTERPRETATIVE REGULATIONS

§ 121.1 *Definitions and interpretations.* (a) "Secretary" means the Secretary of Health, Education, and Welfare.

(b) "Department" means the Department of Health, Education, and Welfare.

(c) "Commissioner" means the Commissioner of Food and Drugs.

(d) As used in this part, the term "act" means the Federal Food, Drug, and Cosmetic Act approved June 25, 1938 (52 Stat. 1040 et seq., as amended; 21 U. S. C. 301-392).

(e) "Food additive" includes all substances the intended use of which results or may reasonably be expected to result, directly or indirectly, either in their becoming a component of food or otherwise affecting the characteristics of food. A material used in the production of containers and packages is subject to the definition if it may reasonably be expected to become a component, or to affect the characteristics, directly or indirectly, of food packed in the container. "Affecting the characteristics of food" does not include physical effects, such as protecting contents of packages, preserving shape, and preventing moisture loss. If there is no migration of a packaging component from the package to the food, it does not become a component of the food and thus is not a food additive. A substance that does not become a component of food, but that is used, for example, in preparing an ingredient of the food to give a different flavor, texture, or other characteristic in the food, may be a food additive.

(f) "Common use in food" refers to usage of a substance by consumers, regardless of the number of manufacturers who may produce it.

(g) "Scientific procedures" include not only original animal, analytical, and other scientific studies, but also a compilation of reliable information drawn from the scientific literature.

(h) "Safe" means that there is convincing evidence that no harm can come from the intended use of the food additive.

§ 121.2 *Pesticide chemicals in processed foods.* When pesticide chemical residues occur in processed foods due to the use of raw agricultural commodities that bore or contained lawful pesticide residues, the processed food will not be regarded as adulterated so long as good manufacturing practice has been followed in removing any residue from the raw agricultural commodity in the processing (such as by peeling or washing) and so long as the concentration of the residue in the processed food when ready to eat is not greater than the tolerance prescribed for the raw agricultural commodity. But when the concentration of residue in the processed food is higher than the tolerance prescribed for the raw agricultural commodity, the processed food is adulterated unless the higher concentration is permitted by a tolerance obtained under section 409 of the act. For example, if fruit bearing a residue of 7 parts per million of DDT, permitted on the raw agricultural commodity is dried and a residue in excess of 7 parts per million of DDT results on the dried fruit, the dehydrated fruit is adulterated unless the higher tolerance for DDT is authorized by the regulations in this part.

§ 121.3 *Substances added to food which are not generally recognized as safe.* (a) In general, any substance added to food which has no history of common use as a food ingredient should be regarded as a substance that is not generally recognized as safe for its intended food use, for the purpose of section 201(s) and 402(a)(2)(C) of the act, unless it has been scientifically tested and shown to be safe.

(b) Section 121.100 contains a partial list of substances that are generally recognized among experts qualified by scientific training and experience to evaluate the safety of such substances as ingredients in food as safe for such use under the conditions set forth in that section. No substance will be removed from this list, nor will the permitted conditions of use be modified, without prior notice and a statement of the reasons for the action.

(c) Substances other than those listed in § 121.100 for which prior sanction under the Federal Food, Drug, and Cosmetic Act has been given, are not listed. Upon written request, setting forth the specific product and a specific usage, the Commissioner will advise interested persons whether such use of such product has been sanctioned. Food additives sanctioned for use in foods for which standards of identity have been prescribed are listed in the standards. No prior sanction will be withdrawn or modified without prior notice and a statement of the reasons for the action.

(d) The Commissioner, upon written request, specifying the intended conditions of use and other pertinent information about a substance, will advise an interested person whether in his opinion the substance is a food additive.

(e) The training and experience necessary to qualify experts to evaluate the safety of food additives, for the purposes of section 201(s) of the act, are essentially sufficient training and experience in biology, medicine, physiology, toxicology, pharmacology, veterinary medicine, or other appropriate science to recognize and to evaluate the behavior and effects of chemical substances in the diet of man and of animals.

§ 121.4 *Tolerances for related food additives.* (a) Food additives that cause related pharmacological effects will be regarded, in the absence of evidence to the contrary, as having additive toxic effects.

(b) Tolerances established for such related food additives may limit the amount of a common component that may be present, or may limit the amount of biological activity (such as cholinesterase inhibition) that may be present, or may limit the total amount of related food additives that may be present.

(c) Where food additives from two or more chemicals in the same class are present in or on a food, the tolerance for the total of such additives shall be the same as that for the additive having the lowest numerical tolerance in this class, unless there are available methods that permit quantitative determination of the amount of each food additive present.

(d) Where residues from two or more additives in the same class are present in or on a food and there are available methods that permit quantitative determination of each residue, the quantity of combined residues that are within the tolerance may be determined as follows:

(1) Determine the quantity of each residue present.

(2) Divide the quantity of each residue by the tolerance that would apply if it occurred alone, and multiply by 100 to determine the percentage of the permitted amount of residue present.

(3) Add the percentages so obtained for all residues present.

(4) The sum of the percentages shall not exceed 100 percent.

§ 121.5 *Generally recognized safety factors to be considered.* In accordance with section 409(c)(5)(C) of the act, the following generally recognized safety factors will be applied in determining whether a proposed use of a food additive will be safe for its intended uses: Except when the circumstances of the particular case require different treatment, a safety ratio based on animal-experiment data of 100 to 1 will be applied; that is, a food additive will not be granted a tolerance that will exceed 1/100 of the maximum amount demonstrated to be without harm to experimental animals.

§ 121.6 *General principles for the evaluation of the safety of food additives.* (a) Unless evidence is available establishing that a different method and procedure will give equally or more reliable results, the Commissioner in reaching a decision on any petition filed under section 409 of the act will apply the applicable criteria for establishing the safety of food additives as outlined by the Food Protection Committee of the National Research Council in its publication entitled "Principles and Procedures for Evaluating the Safety of Intentional Chemical Additives in Foods" (January 1957 Edition). For the purposes of this section, the criteria set forth in the above-referenced publication for the evaluation of intentional additives in food will apply equally to any substance that may properly be classified within the meaning of that term as it is defined in section 201(s) of the act.

(b) Upon written request describing the proposed use of an additive and the proposed experiment to determine its safety, the Commissioner will advise a person who wishes to establish the safety of a food additive, whether he believes an experimental plan that is not in accord with the general guides of the pamphlet described in paragraph (a) of this section, will furnish data adequate for an evaluation of the safety of the additives.

§ 121.7 *Food additives for which new-drug applications are required.* (a) A substance that is a new drug within the meaning of section 201(p) of the act may also be a food additive within the meaning of section 201(s) by reason of the fact that its intended use results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of a food. Any new drug that is intended for administration to a food-

producing animal will also be evaluated under section 409 and a regulation issued where necessary. Where a substance is both a new drug and a food additive, the submission of a new-drug application in accordance with the regulations appearing in Part 130 of this Chapter will also be construed as a petition for the establishment of a regulation for the use of the substance as a food additive. A new-drug application will not be permitted to become effective for a use that results in the substance becoming a food additive until a regulation is established under section 409 of the act. The new-drug application and the establishment of a regulation respecting the food additive use will be acted upon simultaneously.

(b) With respect to those uses of a new drug that result in its becoming a food additive, the provisions of these regulations shall apply concerning the procedure to be followed in establishing a food-additive regulation. Upon determination that a new-drug application contains a petition for the establishment of a food-additive regulation, the New Drug Branch of the Food and Drug Administration shall so notify the applicant prior to the effective date of the application, and shall inform him that his application with respect to the uses of the new drug which result in its becoming a food additive will be processed under the regulations in this part. Upon the issuance of the food-additive regulation, the New Drug Branch will notify the applicant that his application is effective to the extent allowed by the regulation. In the event the proceeding for the food-additive regulation results in the denial of a regulation allowing the use of the new drug as a food additive, the applicant shall be notified that the denial of his new-drug application is final with respect to the use of the new drug for uses resulting in its becoming a food additive.

§ 121.8 *Food additives proposed for use in foods for which definitions and standards of identity have been prescribed.* (a) Where a petition is received for the issuance or amendment of a regulation establishing a definition and standard of identity for a food under section 401 of the act, which proposes the inclusion of a food additive in such definition and standard of identity, the provisions of the regulations in this part shall apply with respect to the information that must be submitted with respect to the food additive. Since section 409(b)(5) of the act requires that the Secretary publish notice of a petition for the establishment of a food-additive regulation within 30 days after filing, notice of a petition relating to a definition and standard of identity shall also be published within that time limitation if it includes a request, so designated, for the establishment of a regulation pertaining to a food additive.

(b) If a petition for a definition and standard of identity contains a proposal for a food-additive regulation, and the petitioner fails to designate it as such, the Commissioner, upon determining that the petition includes a proposal for a food-additive regulation, shall so notify the petitioner and shall thereafter proceed in accordance with the regulations in this part.

(c) A regulation will not be issued allowing the use of a food additive in a food for which a definition and standard of identity is established, unless the evidence demonstrates that the use of such food additive in the standardized food will promote honesty and fair dealing in the interest of consumers.

§121.51 *Petitions proposing regulations for food additives.* (a) Petitions to be filed with the Commissioner under the provisions of section 409(b) of the act shall be submitted in triplicate. If any part of the material submitted is in a foreign language, it shall be accompanied by an accurate and complete English translation. The petition shall state petitioner's post-office address to which published notices or orders issued or objections filed pursuant to section 409 of the act may be sent.

(b) Pertinent information may be incorporated in, and will be considered as part of, a petition on the basis of specific reference to such information submitted to and retained in the files of the Food and Drug Administration. However, any reference to information furnished by a person other than the applicant will not be considered unless use of such information is authorized in a written statement signed by the person who submitted it.

(c) Petitions shall include the following data and be submitted in the following form:

_____
(Date)

Name of petitioner _____

Post-office address _____

Date _____

Name of food additive and proposed use _____

_____

_____

Food and Drug Administration
Department of Health, Education, and Welfare
Washington 25, D. C.

Dear Sirs:

The undersigned, _____, submits this petition pursuant to section 409(b)(1) of the Federal Food, Drug, and Cosmetic Act with respect to the _____.
(name of the food additive and proposed use)

Attached hereto, in triplicate, and constituting a part of this petition, are the following:

A. The name and all pertinent information concerning the food additive, including chemical identity and composition of the food additive, or a statement that such information is not available and why it is not.

[When the chemical identity and composition of the food additive is not known, the petition shall contain information in sufficient detail to permit evaluation regarding the method of manufacture and the analytical controls used during the various stages of manufacturing, processing, or packing of the food additive which are relied upon to establish that it is a substance of reproducible composition. Alternative methods and controls and variations in methods and controls within reasonable limits that do not affect the characteristics of the substance or the reliability of the controls may be specified.

[If the food additive is a mixture of chemicals, the petition shall supply a list of all substances used in the syntheses, extraction, or other method of preparation, regardless of whether they undergo chemical change in the process. Each substance should be identified by its common English name and complete chemical name, using structural formulas when necessary for specific identification. If any proprietary preparation is used as a component, the proprietary name should be followed by a complete quantitative statement of composition. Reasonable alternatives for any listed substance may be specified.

[If the petitioner does not himself perform all the manufacturing, processing, and packing operations for a food additive, the petition shall identify each person who will perform a part of such operations and designate the part.

[If the food additive is one that is likely to be unstable, the petition shall include stability data, and, if needed to preserve the identity, strength, quality, and purity of the additive, an expiration date that will be employed.]

B. The amount of the food additive proposed for use and the purposes for which it is proposed, together with all directions, recommendations, and suggestions regarding the proposed use, as well as specimens of the labeling proposed for the food additive and any labeling that will be required by applicable provisions of the Federal Food, Drug, and Cosmetic Act on the finished food.

[Typewritten or other draft-labeling copy will be accepted for consideration of the petition, provided a statement is made that final printed labeling identical in content to the draft copy will be submitted as soon as available and prior to the marketing of the food additive.

[If the food additive is one for which a tolerance limitation is required to assure its safety, the level of use proposed should be no higher than the amount reasonably required to accomplish the intended physical or other technical effect, even though the safety data may support a higher tolerance.]

C. Data establishing that the food additive will have the intended physical or other technical effect and the amount necessary to accomplish this. These data should include information in sufficient detail to permit evaluation with control data.

D. The results of tests by practicable methods to determine the amount of the food additive in the finished food and of any substance formed in or on food because of its use. The test proposed shall be one that can be used for food-control purposes and that can be applied with consistent results by various laboratories.

E. Full reports of investigations made with respect to the safety of the food additive.

[A petition may be regarded as incomplete unless it includes full reports of adequate tests by all methods reasonably applicable to show whether or not the food additive will be safe for its intended use. The reports ordinarily should include detailed data derived from appropriate animal and other biological experiments in which the methods used and the results obtained are clearly set forth. The petition shall not omit without explanation any reports of investigations that would bias an evaluation of the safety of the food additive.]

F. Proposed tolerances for the food additive, if tolerances are required in order to insure its safety.

G. If submitting petition to modify an existing regulation issued pursuant to section 409(c)(1)(A) of the act, full information on each proposed change that is to be made in the original regulation must be submitted. The petition may omit statements made in the original petition concerning which no change is proposed. A supplemental petition must be submitted for any change beyond the variations provided for in the original petition and the regulation issued on the basis of the original petition.

H. It is understood that all representations in the petition regarding the name, composition, manufacturing methods, controls, and labeling will apply to the food additive when it is actually produced and marketed, until an effective supplement to the petition provides for a change in the food additive.

Yours very truly,

Petitioner .....

By .....

[Indicate authority]

(d) The petitioner will be notified of the date on which his petition is filed, and an incomplete petition, or one that has not been submitted in triplicate, will usually be retained but not filed as a petition under section 409 of the act. The petitioner will be notified in what respects his petition is incomplete.

(e) The petition must be signed by the petitioner or by his attorney or agent, or (if a corporation) by an authorized official.

(f) The data specified under the several lettered headings should be submitted on separate sheets or sets of sheets, suitably identified. If such data have already been submitted with an earlier application, the present petition may incorporate it by specific reference to the earlier. If part of the data have been submitted by the manufacturer of the food additive as a master file, the petitioner may refer to the master file if he obtains the manufacturer's written permission to do so. The manufacturer may authorize specific reference to the data without disclosure to the petitioner.

(g) A petition shall not be accepted for filing if any of the data prescribed by section 409(b)(2) of the act are lacking or are not set forth so as to be readily understood.

(h) Data in a petition will be held confidential and not revealed unless it is necessary to do so in administrative or judicial proceedings under section 409 of the act.

(i)(1) Within 15 days after receipt the Commissioner will notify the petitioner of acceptance or nonacceptance of a petition, and if not accepted the reasons therefor. If accepted, the date of notification becomes the date of filing for the purposes of section 409(b)(5) of the act. If the petitioner desires, he may supplement a deficient petition after being notified regarding deficiencies. If the supplementary material or explanation of the petition is deemed acceptable, petitioner shall be notified, and date of such notification becomes the date of filing. If the petitioner does not wish to supplement or explain the petition and requests in writing that it be filed as submitted, the petition shall be filed and the petitioner so notified. The date of such notification becomes the date of filing.

(2) The Commissioner will publish in the FEDERAL REGISTER within 30 days from the date of filing of such petition a notice of filing, the name of petitioner, and a brief summary of the petition in general terms.

(j) The Commissioner may request a full description of the methods used in, and the facilities and controls used for the production of the food additive, or a sample of the food additive, or articles used as components thereof, or of the food in which the additive is proposed to be used, at any time while a petition is under consideration. The Commissioner shall specify in the request for a sample of the food additive, a quantity deemed adequate to permit tests of analytical methods to determine quantities of the food additive present in foods for which it is intended to be used. The date used for computing the 90-day limit for the purposes of section 409(c)(2) of the act shall be moved forward 1 day for each day after the mailing date of the request taken by the petitioner to submit the sample. If the information or sample requested is not submitted within 180 days after filing of the petition, the petition will be considered withdrawn without prejudice.

(k) The Commissioner will forward for publication in the FEDERAL REGISTER, within 90 days after filing of the petition (or within 180 days if the time is extended as provided for in section 409(c)(2) of the act), a regulation prescribing the conditions under which the food additive may be safely used (including, but not limited to, specifications as to the particular food or classes

of food in or on which such additive may be used, the maximum quantity that may be used or permitted to remain in or on such food, the manner in which such additive may be added to or used in or on such food, and any directions or other labeling or packaging requirements for such additive deemed necessary by him to assure the safety of such use), and shall notify the petitioner of such order and the reasons for such action; or by order deny the petition, and shall notify the petitioner of such order and of the reasons for such action.

(1) If the Commissioner determines that additional time is needed to study and investigate the petition, he shall by written notice to the petitioner extend the 90-day period for not more than 180 days after the filing of the petition.

§ 121.52 *Withdrawal of petitions without prejudice.* In some cases the Commissioner will notify the petitioner that the petition, while technically complete, is inadequate to justify the establishment of a regulation or the regulation requested by petitioner. This may be due to the fact that the data are not sufficiently clear or complete. In such cases, the petitioner may withdraw the petition pending its clarification or the obtaining of additional data. This withdrawal will be without prejudice to a future filing. Upon refiling, the time limitation will begin to run anew from the date of refiling.

§ 121.53 *Substantive amendments to petitions.* After a petition has been filed, the petitioner may submit additional information or data in support thereof, but in such cases the petition will be given a new filing date and the time limitation will begin to run anew.

§ 121.54 *Effective date.* A regulation published in accordance with § 121.7(b) or § 121.72 shall become effective upon publication in the FEDERAL REGISTER.

§ 121.55 *Objections to regulations and requests for hearings.* (a) Objections to an order promulgated pursuant to section 409(f)(1) of the act shall be submitted in quintuplicate to the Hearing Clerk of the Department at the address specified in such order. Each objection to a provision of the regulation shall be separately numbered.

(b) A statement of objections shall not be accepted for filing if:

(1) It is filed more than 30 days after the date of publication of the order in the Federal Register.

(2) It fails to establish that the objector will be adversely affected by the regulation.

(3) It does not specify with particularity the provisions of the regulation to which objection is taken.

(4) It does not state reasonable grounds for each objection raised. Grounds that it is reasonable to conclude are capable of being established by reliable evidence at the hearing, and which if proved would call for changing the provisions specified in the objections, will be deemed reasonable grounds.

(c) If the statement of objections may not be filed, the Commissioner shall inform the objector of the reasons.

(d) If objections to a regulation issued pursuant to the filing of a petition are filed by a person other than the petitioner, the Food and Drug Administration shall send a copy of the objections by certified mail to the petitioner at the address given in the petition. Petitioner shall have 2 weeks from the date of receipt by him of the objections to make written reply.

§ 121.56 *Public hearing; notice.* If the objections and statements filed by any person, when they are considered with the record in the proceeding (including any reply to the objections that the petitioner may have filed), show that the

person filing the objections is adversely affected and that the grounds stated in support of the objections are reasonable, and a public hearing on the objections is requested, the Commissioner shall cause to be published in the FEDERAL REGISTER a notice reciting the objections and announcing a public hearing to receive evidence on them. The notice shall designate the place where the hearing will be held, specify the time within which appearances must be filed, and specify the time (not earlier than 30 days after the date of publication of the notice in the Federal Register) when the hearing will commence. The hearing shall convene at the place and time announced in the notice, but thereafter it may be moved to a different place and may be continued from day to day or recessed to a later day without other notice than announcement thereof by the presiding officer at the hearing. Included in such notice shall be a statement indicating whether the regulation to which objection was taken shall be stayed pending the outcome of the hearing.

§ 121.57 *Presiding officer.* The hearing shall be conducted by a presiding officer, who shall be a hearing examiner appointed as provided in the Administrative Procedure Act (sec. 7, 60 Stat. 237, as amended; 5 U. S. C. 1007 et seq.) and designated by the Commissioner for conducting the hearing. Any such designation may be made or revoked by the Commissioner at any time. Hearings shall be conducted in an informal but orderly manner in accordance with the regulations of this part and the requirements of the Administrative Procedure Act. The presiding officer shall have the power to administer oaths and affirmations, to rule upon offers of proof and admissibility of evidence, to receive relevant evidence, to examine witnesses, to regulate the course of the hearing, to hold conferences for the simplification of the issues, and to dispose of procedural requests; but he shall not have power to decide any motion that involves final determination of the merits of the proceeding.

§ 121.58 *Parties; burden of proof; appearances.* At the hearing, the person whose objections raised the issues to be determined shall be, within the meaning of section 7(c) of the Administrative Procedure Act, the proponent of the order sought, and accordingly shall have the burden of proof. Any interested person shall be given an opportunity to appear at the hearing, either in person or by his authorized representative, and to be heard with respect to matters relevant to the issues raised by the objections. Any interested person who desires to be heard at the hearing in person or through a representative shall, within the time specified in the notice of hearing, file with the presiding officer a written notice of appearance setting forth his name, address, and employment. If such person desires to be heard through a representative, such person or such representative shall file with the presiding officer a written appearance setting forth the name, address, and employment of such person. Any person or representative shall state with particularity in the notice of appearance his interest in the proceedings and shall set forth the specific provisions of the regulations concerning which objections have been made on which such person desires to be heard. The notice of appearance shall also set forth with particularity the position to be taken concerning the objections on which he wishes to be heard. No person shall be heard if he failed to file notice of his appearance within the time prescribed, in the absence of a clear showing of good cause why the notice of appearance was not filed. All present at the hearing shall conform to all reasonable standards of orderly and ethical conduct.

§ 121.59 *Request for stay of effectiveness of regulation pending a hearing.* When a hearing is requested under § 121.55, the request may also include a request for a stay of effectiveness of the order (§ 121.59), in whole or in part, which request

shall include the reasons for the stay together with a showing that the stay involves no hazard to the public health.

§ 121.60 *Prehearing and other conferences.* (a) The presiding officer, on his own motion or on the motion of any party or his representative, may direct all parties or their representatives to appear at a specified time and place for a prehearing conference to consider:

(1) The simplification of the issues.

(2) The possibility of obtaining stipulations, admissions of facts, and documents.

(3) The limitation of the number of expert witnesses.

(4) The scheduling of witnesses to be called.

(5) The advance submission of all documentary evidence.

(6) Such other matters as may aid in the disposition of the proceeding.

The presiding officer shall make an order reciting the action taken at the conference, the agreements made by the parties or their representatives, and the scheduling of witnesses, and limiting the issues for hearing to those not disposed of by admissions or agreements. Such order shall control the subsequent course of the proceeding unless modified for good cause by subsequent order.

(b) The presiding officer may also direct all parties and their representatives to appear at conferences at any time during the hearing with a view to simplification, clarification, or shortening of the hearing.

§ 121.61 *Submission of documentary evidence in advance of hearing.* (a) All documentary evidence to be offered at the hearing shall be submitted to the presiding officer and to the interested parties sufficiently in advance of the offer of such documentary evidence for introduction into the record to permit study and preparation of cross-examination and rebuttal evidence.

(b) The presiding officer, after consultation with the parties at a conference called in accordance with § 121.60 shall make an order specifying the time at which documentary evidence shall be submitted. He shall also specify in his order the time within which objection to the authenticity of such documents must be made to comply with paragraph (d) of this section.

(c) Documentary evidence not submitted in advance in accordance with the requirements of paragraphs (a) and (b) of this section shall not be received in evidence in the absence of a clear showing that the offering party had good cause for his failure to produce the evidence sooner.

(d) The authenticity of all documents submitted in advance shall be deemed admitted unless written objection thereto is filed with the presiding officer upon notice to the other parties within the time specified by the presiding officer in accordance with paragraph (b) of this section, except that a party will be permitted to challenge such authenticity at a later time upon a clear showing of good cause for failure to have filed such written objection.

§ 121.62 *Excerpts from documentary evidence.* When portions only of a document are to be relied upon, the offering party shall prepare the pertinent excerpts, adequately identified, and shall supply copies of such excerpts, together with a statement indicating the purpose for which such materials will be offered, to the presiding officer and to the other parties. Only the excerpts, so prepared and submitted, shall be received in the record. However, the whole of the original document should be made available for examination and for use by opposing counsel for purposes of cross-examination.

§ 121.63 *Submission and receipt of evidence.* (a) Each witness shall, before proceeding to testify, be sworn or make affirmation.

(b) When necessary to prevent undue prolongation of the hearing, the presiding officer may limit the number of times any witness may testify, the repetitious examination and cross-examination of witnesses, or the amount of corroborative or cumulative evidence.

(c) The presiding officer shall admit only evidence which is relevant, material, and not unduly repetitious.

(d) Opinion evidence shall be admitted when the presiding officer is satisfied that the witness is properly qualified.

(e) The presiding officer shall file as an exhibit a copy of the FEDERAL REGISTER promulgating the regulation to which objections were taken and the objections that form the basis for the hearing. All documents constituting the record bearing on the point in controversy, and not entitled to protection under section 301(j) of the act, accumulated up to the start of the hearing shall be open for inspection by interested persons during office hours in the office of the Hearing Clerk of the Department, Room 5440, 330 Independence Avenue SW., Washington 25, D. C.

(f) If any person objects to the admission or rejection of any evidence or to other limitation of the scope of any examination or cross-examination, he shall state briefly the grounds for such objection, and the transcript shall not include extended argument or debate thereon except as ordered by the presiding officer. A ruling of the presiding officer on any such objection shall be a part of the transcript, together with such offer of proof as has been made.

§ 121.64 *Transcript of the testimony.* Testimony given at a public hearing shall be reported verbatim. All written statements, charts, tabulations, and similar data offered in evidence at the hearing shall be marked for identification and, upon a showing satisfactory to the presiding officer of their authenticity, relevancy and materiality, shall be received in evidence subject to the Administrative Procedure Act (sec. 7(c), 60 Stat. 238; 5 U. S. C. 1008(c)). Exhibits shall, if practicable, be submitted in quintuplicate. In case the required number of copies are not made available, the presiding officer shall exercise his discretion in determining whether said exhibit shall be read in evidence or whether additional copies shall be required to be submitted within a time to be specified by the presiding officer. Where the testimony of a witness refers to a statute, or to a report or document, the presiding officer shall, after inquiry relating to the identification of such statute, report, or document, determine whether the same shall be produced at the hearing and physically be made a part of the evidence by reference. Where relevant and material matter offered in evidence is embraced in a report or document containing immaterial and irrelevant matter, such immaterial and irrelevant matter shall be excluded and shall be segregated insofar as practicable, subject to the direction of the presiding officer.

§ 121.65 *Oral and written arguments.* (a) Unless the presiding officer issues an announcement at the hearing authorizing oral argument before him, it shall not be permitted.

(b) The presiding officer shall announce at the hearing a reasonable period within which interested persons may file written arguments based solely upon the evidence received at the hearing, citing the pages of the transcript of the testimony or properly identified exhibits where such evidence occurs.

§ 121.66 *Indexing of record.* (a) Whenever it appears to the presiding officer that the record of hearing will be of such length that an index to the record will permit a more orderly analysis of the evidence and reduce delay, the presiding officer shall require counsel for the parties to prepare a daily topical

index, which will be available to the presiding officer and all parties. Preparation of such an index shall be apportioned among all counsel present in such manner as appears just and proper in the circumstances.

(b) The index shall include each topic of testimony upon which evidence is taken, the name of each witness testifying upon the topic, the page of the record at which each portion of his testimony appeared, and the number of each exhibit relating to the topic. The index shall also contain the name of each witness, followed by the topics upon which he testified and the page of the record at which such testimony appears.

§ 121.67 *Certification of record.* At the close of the hearing, the presiding officer shall afford interested persons a short time (not longer than 1 week, except in unusual cases) in which to point out errors that may have been made in transcribing the testimony. The presiding officer shall promptly thereafter order such corrections made as in his judgment are required to make the transcript conform to the testimony, and he shall certify the transcript of testimony and the exhibits to the Commissioner.

§ 121.68 *Filing the record of the hearing.* As soon as practicable after the close of the hearing, the complete record of the hearing shall be filed in the office of the Hearing Clerk. The record shall include the transcript of the testimony, all exhibits, and any written arguments that may have been filed.

§ 121.69 *Copies of the record of the hearing.* The Department will make provision for a stenographic record of the testimony and for such copies of the transcript thereof as it requires for its own purposes. Any person desiring a copy of the record of the hearing or of any part thereof shall be entitled to the same upon payment of the costs thereof.

§ 121.70 *Proposed order after public hearing.* As soon as practicable after the time for filing written arguments has ended, the Commissioner shall prepare and cause to be published in the FEDERAL REGISTER a proposed order which shall set forth in detail the findings of fact and conclusions, and recommend decision on the objections that were the subject of the hearing and tentative regulations. The proposed order shall specify a reasonable time, ordinarily not to exceed 30 days, within which any interested person may file exceptions. The exceptions shall point out with particularity the alleged errors in said proposed order and shall contain a specific reference to the pages of the transcript of the testimony or to the exhibits on which each exception is based. Such exceptions may be accompanied by a memorandum or brief.

§ 121.71 *Final order after public hearing.* As soon as practicable after the time for filing exceptions has passed, the record and the exceptions shall be presented to the Secretary and he shall cause to be published in the FEDERAL REGISTER his final order promulgating the regulation, which shall specify the date on which the order shall take effect.

§ 121.72 *Adoption of regulation on initiative of Commissioner.* (a) The Commissioner upon his own initiative may propose the issuance of a regulation prescribing, with respect to any particular use of a food additive, the conditions under which such additive may be safely used. Notice of such proposal shall be published in the FEDERAL REGISTER and shall state the reasons for the proposal.

(b) Action upon a proposal made by the Commissioner shall, after publication of the notice, proceed as provided in § 121.51.

§ 121.73 *Judicial review.* The Commissioner hereby designates the Assistant General Counsel for Food and Drugs of the Department of Health, Education,

and Welfare as the officer upon whom copy of petition for judicial review shall be served. Such officer shall be responsible for filing in the court a transcript of proceedings and the record on which the order of the Secretary of Health, Education, and Welfare is based. The transcript and record shall be certified by the Secretary.

§ 121.74 *Procedure for amending and repealing tolerances or exemptions from tolerances.* The Commissioner on his own initiative, or on request from an interested person furnishing reasonable grounds therefor, may propose the issuance of a regulation amending or repealing a regulation pertaining to a food additive or granting or repealing an exemption for such additive. Requests for such amendment or repeal shall be made in writing.

(b) "Reasonable grounds" shall include an explanation showing wherein the person has a substantial interest in such regulation and an assertion of facts (supported by data if available) showing that new information exists with respect to the food additive or that new uses have been developed or old uses abandoned, that new data are available as to toxicity of the chemical, or that experience with the existing regulation or exemption may justify its amendment or repeal. New data should be furnished in the form specified in § 121.51 for submitting petitions.

(c) The notice announcing the proposal to amend or repeal a regulation shall show whether the proposal was made on the initiative of the Commissioner or at the request of an interested person, naming such person. From this point, the proceedings shall be the same as prescribed by the regulations in this part and by section 409(b) of the act, for the issuance of a regulation.

SUBPART B—EXEMPTION OF CERTAIN FOOD ADDITIVES FROM THE REQUIREMENT OF TOLERANCES

§ 121.100 *Substances that are generally recognized as safe.* It is impractical to list all substances that are generally recognized as safe for their intended use. However, by way of illustration, the Commissioner regards such common food ingredients as salt, pepper, sugar, vinegar, baking powder, and monosodium glutamate as safe for their intended use. In addition, the following lists include some substances that, when used for the purposes indicated, in accordance with good food manufacturing practice, are regarded by the Commissioner as generally recognized as safe for such uses.

BUFFERS AND NEUTRALIZING AGENTS

Acetic acid
Aluminum ammonium sulfate
Aluminum sodium sulfate
Aluminum potassium sulfate
Ammonium bicarbonate
Ammonium carbonate
Ammonium hydroxide
Ammonium phosphate (mono- and dibasic-)
Calcium carbonate
Calcium chloride
Calcium citrate
Calcium gluconate
Calcium hydroxide
Calcium lactate
Calcium oxide
Calcium phosphate
Citric acid
Lactic acid
Linoleic acid
Magnesium carbonate
Magnesium oxide
Oleic acid
Potassium acid tartrate
Potassium bicarbonate
Potassium carbonate
Potassium citrate
Potassium hydroxide
Sodium acetate
Sodium acid pyrophosphate
Sodium aluminum phosphate
Sodium bicarbonate

Sodium carbonate
Sodium citrate
Sodium hydroxide
Sodium phosphate (mono-, di-, tri-)
Sodium potassium tartrate
Sodium sesquicarbonate
Sulfuric acid
Tartaric acid

COLORS

Caramel
Carbon black
Charcoal
Titanium dioxide
Ultramarine blue

PRESERVATIVES

Sequestrants

Calcium acetate
Calcium chloride
Calcium citrate
Calcium diacetate
Calcium gluconate
Calcium hexametaphosphate
Calcium phytate
Citric acid
Dipotassium phosphate
Disodium phosphate
Monocalcium acid phosphate
Monoisopropyl citrate
Potassium citrate
Sodium acid phosphate
Sodium citrate
Sodium diacetate
Sodium gluconate
Sodium hexametaphosphate
Sodium metaphosphate
Sodium phosphate (mono-, di-, tribasic-)
Sodium potassium tartrate
Sodium pyrophosphate
Sodium tartrate
Sodium tetrapyrophosphate
Sodium tripolyphosphate
Tartaric acid

Antimycotics

Calcium proprionate
Potassium sorbate
Propionic acid
Sodium proprionate
Sodium sorbate
Sorbic acid

Antioxidants

Ascorbic acid
Ascorbyl palmitate
Calcium ascorbate
Erythorbic acid
Sodium ascorbate
Tocopherols

General

Acetic acid
Citric acid
Phosphoric acid
Sorbitol

MISCELLANEOUS

Aluminum sodium sulfate
Aluminum sulfate
Butane
Calcium phosphate, tribasic
Carbon dioxide
Carnauba wax
Glycerin
Glycerol monostearate
Helium
Magnesium carbonate
Magnesium hydroxide
Monoammonium glutamate
Nitrogen
Papain
Propane
Propylene glycol
Triacetin (glyceryl triacetate)
Tricalcium phosphate

Sodium carbonate
Sodium phosphate
Sodium polyphosphate

NONNUTRITIVE SWEETENERS

Calcium cyclohexyl sulfamate
Sodium saccharin
Saccharin
Sodium cyclohexyl sulfamate
Sodium saccharin

NUTRIENTS

Ascorbic acid
Calcium carbonate
Calcium oxide
Calcium pantothenate
Calcium phosphate (mono-, di-, tribasic)
Calcium sulfate
Carotene
Ferric phosphate
Ferric pyrophosphate
Ferric sodium pyrophosphate
Ferrous sulfate
Iron, reduced
l-lysine monohydrochloride
Niacin
Niacinamide
D-Pantothenyl alcohol
Potassium chloride
Pyridoxine hydrochloride
Riboflavin
Riboflavin-5-phosphate
Sodium pantothenate
Sodium phosphate (mono-, di-, tribasic)
Thiamine hydrochloride
Thiamine mononitrate
Tocopherols
a-tocopherol acetate
Vitamin A
Vitamin A acetate
Vitamin A palmitate
Vitamin B_{12}
Vitamin D_2
Vitamin D_3

STABILIZERS

Agar-agar
Carob bean
Carragheen
Guar gum

EMULSIFYING AGENTS

Acetyl tartaric acid esters of mono- and diglycerides, except lauric
Mono- and diglycerides, except lauric
Monosodium phosphate derivatives of mono- and diglycerides, except lauric
Propylene glycol

MISCELLANEOUS

Product	*Tolerance*	*Uses*
Aluminum calcium silicate	2%	Table salt
Calcium silicate	5%	As an anticaking agent in baking powder
Calcium silicate	2%	As an anticaking agent in table salt
Caffeine	⅓ to ½-grain in 6-oz. bottles of cola drinks	In cola drinks

Product	*Tolerance*	*Uses*
Ethyl formate	15 parts per million	When used as fumigant for cashew nuts
Magnesium silicate	2%	Table salt; anticaking agent
Ox Bile Extract U. S. P. (solids)	0.01%	Egg whites
Taurocholic acid (or its sodium salt)	0.01%	do.
Tricalcium silicate	2%	As an anticaking agent in table salt
Triethyl citrate	0.25%	Egg whites
NUTRIENTS		
Copper gluconate	0.005%	In any food
Cuprous iodide	0.01%	Used in table salt as source of dietary iodine
Potassium iodide	0.01%	do.
PRESERVATIVES		
Antimycotics		
Caprylic acid	.....	Antimycotic in cheese wraps
Potassium bisulfite	.....	Not in meats or in foods recognizable as a source of vitamin B_1
Potassium metabisulfite	.....	do.
Sodium benzoate	0.1%	No special use specified
Sodium bisulfite	.....	Not in meats or in foods recognizable as a source of vitamin B_1
Sodium metabisulfite	.....	do.
Sodium sulfite	.....	do.
Antioxidants		
Benzoic acid	0.1%	No special use specified
Butylated hydroxytoluene	0.02%	Edible fats and oils
Butylated hyroxyanisole	0.02%	do.
Dilauryl thiodipropionate	0.02%	do.
Gum guaiac	0.1%	do.
Nordihydroguaiaretic acid	0.02%	do.
Propyl gallate	0.02%	do.
Thiodipropionic acid	0.02%	do.
General		
Sulfur dioxide	.....	Not in meats or in foods recognizable as a source of vitamin B_1
Sequestrants		
Isopropyl citrate	0.02%	No special use specified
Sodium thiosulfate	0.1%	Salt
Stearyl citrate	0.15%	No special use specified

STABILIZERS

Magnesium stearate	.....	As migratory substance; use in manufacturing plastic film in wrapping foods

SURFACTANTS

Cholic acid	0.01%	Egg white
Desoxycholic acid	0.01%	do.
Glycocholic acid	0.01%	do.

Dated: December 3, 1958

GEO. P. LARRICK,
Commissioner of Food and Drugs

REPORTS TO THE READER—Continued from page 740

Other distinguished guests seated at the head table were John W. Gwynne, Chairman of the Federal Trade Commission; Joseph P. O'Hara, James J. Delaney, A. L. Miller and Oren Harris, Members of Congress (Mr. Harris is chairman of the House Committee on Interstate and Foreign Commerce); Paul S. Willis, president, Grocery Manufacturers of America; Edith H. Sherrard, associate, social and economic issues, American Association of University Women; Faith Fenton, of Cornell University, representing the American Home Economics Association; Alyce Shary, consumer chairman, General Federation of Women's Clubs; Dean William C. Warren, of Columbia University School of Law; Sally Butler, research director, General Federation of Women's Clubs; and Major General Dan C. Ogle, Surgeon General, United States Air Force.

Also among those attending were John S. Andrews, director of food research, General Mills, Inc.; H. Thomas Austern, counsel, National Canners Association; Bernard E. Conley, secretary, Committee on Toxicology of American Medical Association; Franklin M. Depew, attorney, Standard Brands, Inc.; Frank T. Dierson, secretary, The Food Law Institute; W. E. Fairbanks, general counsel, Thomas J. Lipton, Inc.; A. M. Gilbert, counsel, Best Foods Division, Corn Products Company; E. L. Harding, vice president and general counsel, Kellogg Company; Albert H. Holland, Jr., M. D., Medical Director, FDA; Wallace F. Janssen, Director, Division of Public Information, FDA; Vincent A. Kleinfeld, attorney, Washington, D. C.; J. F. Lakey, secretary, Association of Food and Drug Officials of the United States; Michael F. Markel, Markel & Hill, Washington, D. C.; E. J. Matson, director of scientific relations, Abbott Laboratories; Samuel A. McCain, general counsel, Corn Products Company; A. R. Miller, director, Meat Inspection Division, United States Department of Agriculture; Merrill E. Olsen, vice president and general counsel, Quaker Oats Company; L. I. Pugsley, acting director, Food and Drug Directorate, Canadian Department of National Health and Welfare; Philip F. Sherman, secretary and general counsel, Pillsbury Mills, Inc.; Erwin P. Snyder, general counsel, Kraft Foods Company; A. J. Stokely, executive vice president, Stokely-Van Camp, Inc.; G. Cullen Thomas, consultant, General Mills, Inc.; Edward Brown Williams, attorney, Washington, D. C.; and Julius G. Zimmerman, attorney, The Coca-Cola Export Corporation.

Poultry Additives

The following important list of food additives approved under the Poultry Products Inspection Act and exempted by the 1958 food-additives amendment was received just in time for inclusion in this December JOURNAL. It is presented in full text:

UNITED STATES DEPARTMENT OF AGRICULTURE
Agricultural Marketing Service
Poultry Division
Washington 25, D. C.

November 20, 1958

TO: All Poultry Inspectors, Inspection Branch

FROM: G. S. McKee, Pathology Section Head, Inspection Branch

SUBJECT: PERMITTED FOOD ADDITIVES

Additive	*Purpose*	*Amount*
Acetic acid	Refining	Sufficient for purpose
Amines, filming	Volatile boiler additive to retard corrosion in pipes	See chemical names
Agar Agar	Stabilizer	Sufficient for purpose
Animal & Vegetable Oil	Shortening	Sufficient for purpose
Anti-foam A (methyl polysilicone)	To retard foaming	10 ppm
Antioxidants (oxygen interceptors)	To retard rancidity development	0.01% singly; 0.02% combinations
Ascorbic acid	Accelerate color fixing in curing	7½ ozs. to 100 gals. pickle; ¾ oz. to 100 lbs. chicken meat
Benzoate, sodium; benzoic acid	To retard flavor reversion	0.1%
BHA (butylated hydroxyanisole)	Antioxidant: To retard rancidity development	0.01%
BHT (butylated hydroxytoluene)	Antioxidant: To retard rancidity development	0.01%
Bicarbonate of soda	To neutralize excess acidity; cleaning vegts.	Sufficient for purpose
Caramel	Flavor	Sufficient for purpose
Carbon (purified charcoal)	Refining	Sufficient for purpose
Caseinate, sodium	Binder and extender	Sufficient for purpose
Cellulose gum (carboxymethyl cellulose)	Extender, stabilizer	Sufficient for purpose
Chlortetracycline	To retard spoilage	7 parts per million
Citric acid	Synergist: To increase effectiveness of antioxidants	0.01%
Citric acid and sodium citrate	Prevents coagulation	0.2%
Condiments	To develop flavor	Sufficient for purpose
Sodium chloride (NACL)	Flavoring and deboning process	Sufficient for purpose

Additive	*Purpose*	*Amount*
Coffee extract	To develop flavor	Sufficient for purpose
Coloring material, vegetable and synthetic	Casings and ink only	Sufficient for purpose
Corn syrup	Flavor, cure	2.5%
Corn syrup dried	Flavor, cure	2.0%
Cyclamate, sodium	Sweetener	0.15%
Cyclohexylamine	To retard corrosion	10 ppm from approved feeder
Dextrose	Flavor; cure seasoning	Sufficient for purpose
Diacetyl	Flavor	Sufficient for purpose
Diatomaceous earth	Refining	Sufficient for purpose
Dry ice (carbon dioxide solid)	Cooling	Sufficient for purpose
Enzymes, proteolytic	Soften tissue	Sufficient for purpose
Ficin	Soften tissue	Sufficient for purpose
Flavoring (chemical and synthetic)	Flavor	Sufficient for purpose
Flour (rice, potato, wheat)	Thickener	Sufficient for purpose
Fullers earth	Refining	Sufficient for purpose
Gelatin	Thickener	Sufficient for purpose
Glycerol (glycerine)	Inhibit drying; manufacture of mono & diglycerides	Sufficient for purpose
Glycerol lactopalmitate, etc.	A type of mono- & diglycerides	Sufficient for purpose
Gums, vegetable (Tragacanth, karaya, etc.)	Emulsifying agent; binder	Sufficient for purpose
Hydrolyzed plant protein	Flavor	Sufficient for purpose
Isoascorbic acid	Accelerate color fixing in curing	7½ ozs. to 100 gals. pickle; ¾ ozs. to 100 lbs. chicken meat
Lactic acid	To develop flavor	0.5%
Lecithin	To retard rancidity development; emulsifier	Sufficient for purpose
Lignin	Loosen scale	Sufficient for purpose
Malt syrup	Flavor; cure	2.5%
Mono-and diglycerides	Emulsifiers	Sufficient for purpose
Monoisopropyl citrate	To increase effectiveness of antioxidants	0.01% in lard & shortening
Monosodium glutamate	Flavor	Sufficient for purpose
Nitrate of soda or potassium	Source of nitrite	See Sodium or potassium nitrate
Nitrite of soda or potassium	Fix color	See sodium or potassium nitrite
Nitrogen	Exclude oxygen	Sufficient for purpose
Nordihydroguaiaretic acid (NDGA)	Antioxidant: To retard rancidity development	0.01%
Oxygen interceptors	See antioxidants	
Papain	Soften tissue	Sufficient for purpose

Additive	*Purpose*	*Amount*
Phosphates: disodium; sodium hexameta-; tripoly-; sodium pyro-; sodium acid pyrophosphate	Decrease amount of cooked-out juices	5.0% in pumping pickle; 0.5% in canned chopped chicken
Phosphate, sodium hexameta-	Retard scale formation in pipes	10 ppm from approved feeder
Phosphoric acid	Synergist: To increase effectiveness of antioxidants	0.01%
Propyl gallate	Antioxidant: To retard rancidity development	0.01%
Resin guaiac	Antioxidant: To retard rancidity development	0.1%
Silica gel	Anti-caking agent	0.5%
Sodium ascorbate; sodium isoascorbate	Accelerate color fixing in curing	7½ ozs. to 100 gals. pickle; ⅞ oz. to 100 lbs. chicken meat; 10% soln. to surface of cured product prior to packaging
Sodium bicarbonate	To neutralize excess acidity; cleaning vegts.	Sufficient for purpose
Sodium caseinate	Binder and extender	Sufficient for purpose
Sodium or potassium nitrate	Source of nitrite	7 lbs. to 100 gals. pickle; 3½ ozs. to 100 lbs. chicken meat (dry cure); 2¾ oz. to 100 lbs. chopped chicken meat
Sodium or potassium nitrite	Color fixing	200 ppm (02%) in product; 2 lbs. to 100 gal. pickle; 1 oz. to 100 lbs. chicken meat (dry cure); ¼ oz. to 100 lbs. chopped chicken meat
Sodium sulfoacetate derivatives of mono- and diglycerides	Emulsifier	0.5%
Sorbitol	Retard drying	Sufficient for purpose
Starch	Thickener	Sufficient for purpose
Stearyl citrate	To protect flavor	0.15%
Sugars, approved (sucrose and dextrose)	Flavoring; curing; seasoning	Sufficient for purpose
Tannic acid	Refining; loosen scale	Sufficient for purpose
Tapioca	Thickener	Sufficient for purpose
Tocopherols	Antioxidant: To retard rancidity development	0.03%
Yeast (dry and wet)	Flavor	Sufficient for purpose

The food additives herein listed are permitted for use in official poultry processing plants provided a letter of approval or an approved label and formula is in the official file. These approvals outline specific conditions for use.

Authority for use of food additives is found in Sections 81.52 and 81.130 of the Regulations, and AMS PY-Instruction No. 918-10 Supplement No. 2 Revised 2/13/57.

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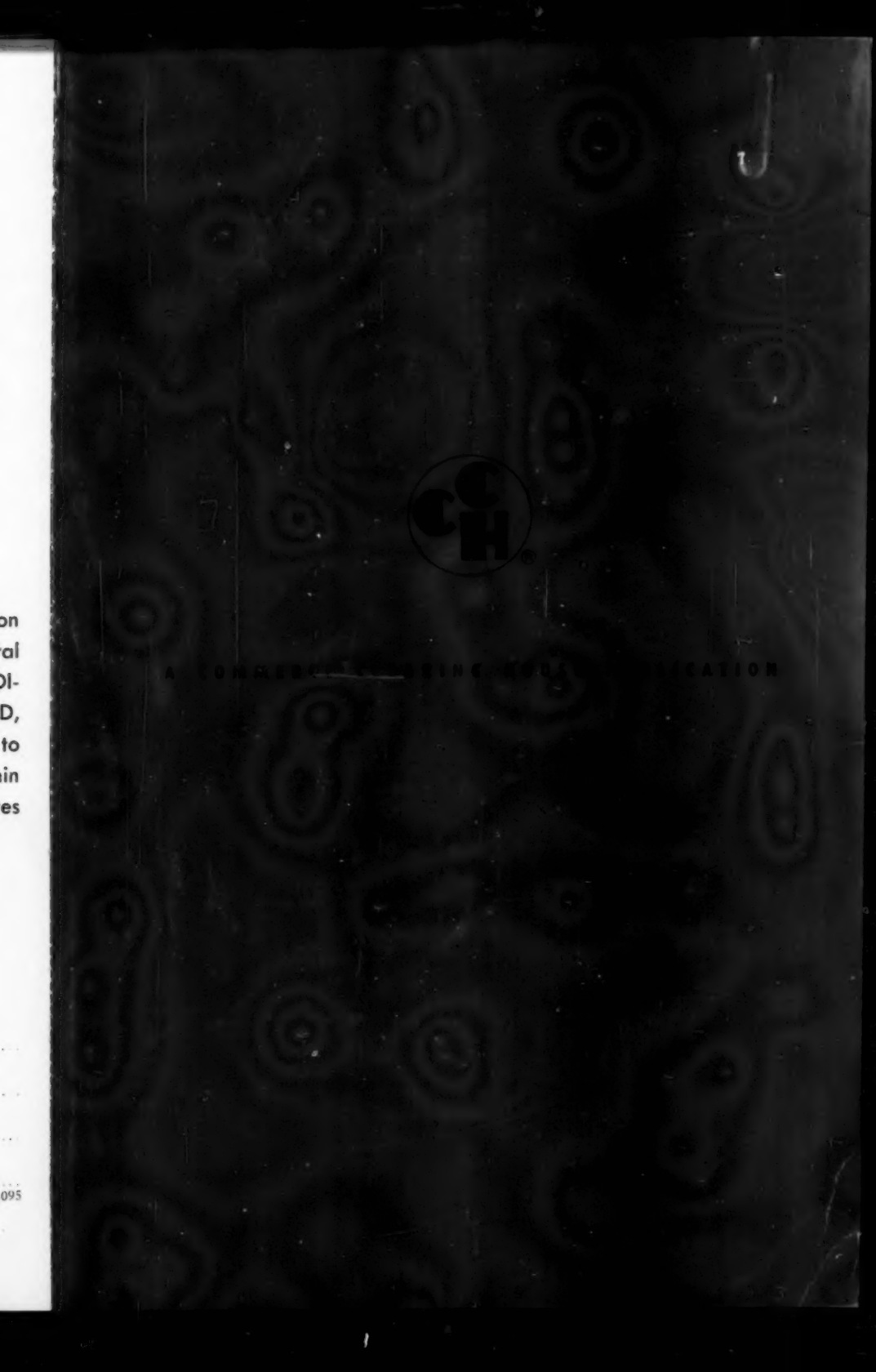
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